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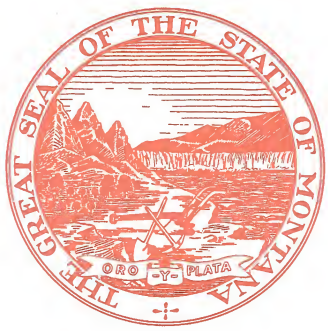
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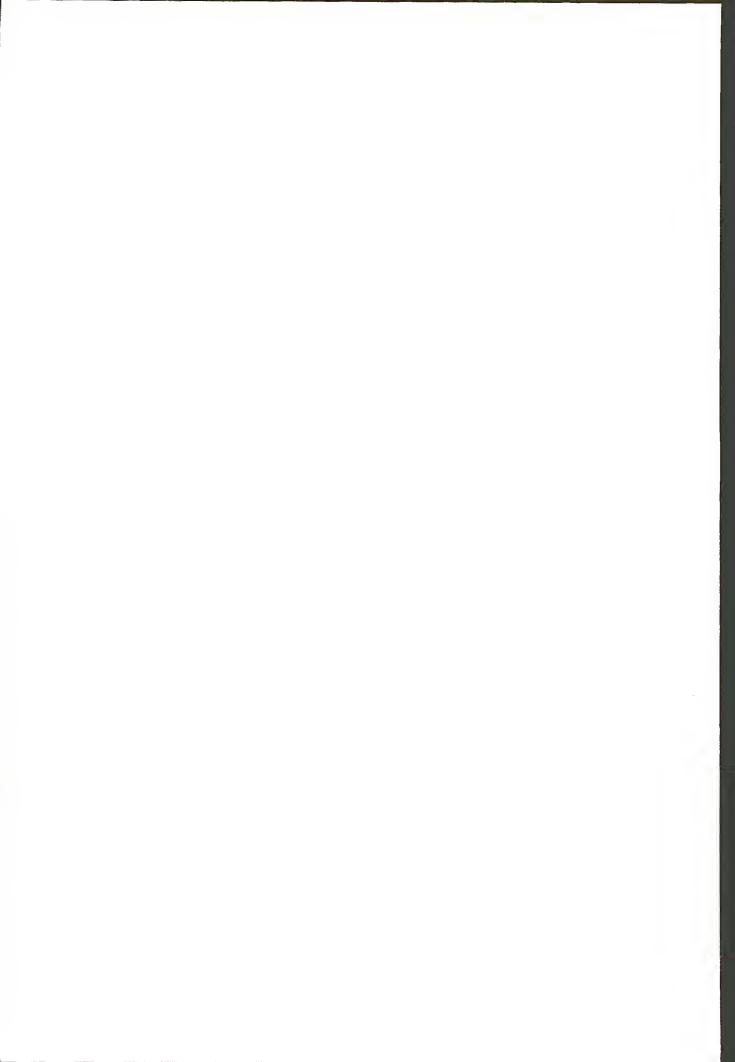


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# IMMUNIZATION CLINIC MANUAL



**Montana Department of Health and  
Environmental Sciences**  
Cogswell Building  
Helena, Montana 59620



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## INTRODUCTION

The Department of Health and Environmental Sciences was created to protect and promote the health of the people of Montana through the implementation of beneficial public health programs and the enforcement of public health laws and regulations. It is the responsibility of the Department staff to assess health care needs and problems in cooperation with local and private sources, to develop and implement the programs designed to meet public health needs and alleviate problems, and to continually evaluate current public health programs.

One of the means of protecting and promoting the health of people is the prevention of illness and death through immunization. Immunization has proven to be a safe and effective way of preventing the morbidity and mortality of many infectious diseases. The low cost and high efficiency of vaccination ensures that every dollar spent on vaccination is repaid many times over because of reduced medical care costs, in addition to lives that remain productive. The Montana Legislature supported this philosophy by passing the Montana School Immunization Law in 1979.

Immunization itself is a complicated subject. It requires knowledge about numerous vaccines, being prepared for the rare side effects, dealing with people in an efficient manner. Control of vaccine-preventable diseases often times requires an extensive knowledge of communicable diseases and maintaining up-to-date information on control measures.

The primary aim of the Montana Immunization Manual is to provide an informative text for public health workers that will be a usable tool that assists us in providing quality immunization services to those in Montana that we serve.

The authors of the manual tried to avoid duplicating information that is available in other resources and at the same time provide reference information that allows cross-checking of related materials. The day-to-day experience of health care workers that deal with immunizations was a valuable resource in determining what is included in the Immunization Manual. The loose leaf format should enable us to maintain a current and ready reference for vaccine-preventable disease and immunization questions.

Thank you to all who responded to draft copies of the Immunization Manual. Your comments were not ignored and will help give it that Montana flavor.

Of course, the manual is only of value if it is used. It is intended for use by administrative, professional and clerical staff that deal with all facets of immunization. The reader should make an effort to recognize how the manual can be used in their clinic setting.



## Program Description and Goals

### Program Description

The Montana Immunization Program supports immunization activities in Montana through vaccine supply, consultation, epidemiologic assistance, training, and organizing and staffing for special immunization clinics.

The Montana Immunization Program functions within the Communicable Disease Section of the Preventive Health Services Bureau which is in the Health Services Division. The Program is staffed by a program manager, three field health officers, an administrative clerk and a public health advisor (when available on assignment to Montana from the Centers for Disease Control). The state epidemiologist is the head of the Communicable Disease Section, the Project Director is the Chief of the Preventive Health Services Bureau. The funding is largely from a grant from the Centers for Disease Control (CDC) with a smaller amount from State general fund.

### Program Goals

The following goals and objectives are the same as those included in the program grant applications.

#### Goals

1. Reduce morbidity and mortality due to vaccine-preventable diseases of childhood.
2. Maintain interruption of indigenous measles transmission.
3. Maintain 90% immunization levels for school children under age 15 against measles, poliomyelitis, diphtheria, tetanus, and rubella. Maintain 95% immunization levels for school enterers and 90% immunization levels for children enrolled in licensed day care centers against measles, poliomyelitis, diphtheria, tetanus, pertussis, rubella, mumps and Haemophilus influenzae type B (Hib) disease.
4. Develop, test and implement systems to insure that 90% or more of children born in Montana complete basic immunization by age two.

#### Long Range Objectives -- 1992

1. By 1992, reported cases of indigenous measles in Montana will be less than five cases per year.
2. By 1992, reported cases of tetanus will be no more than one per year.
3. By 1992, reported cases of diphtheria will be no more than one per year.
4. By 1992, reported cases of pertussis will be less than five per year.
5. By 1992, reported cases of rubella will be maintained at less than five.



6. By 1992, mumps cases will be less than five per year.
7. By 1992, increase reported immunization levels of children under 18 years of age in Montana against measles, polio, diphtheria, pertussis (under 7 years), tetanus, and rubella to equal or greater than 95%.
8. By 1992, increase reported immunization levels of school entering children in Montana against mumps to equal or greater than 95%.
9. By 1992, increase reported immunization levels of children attending licensed day care centers in Montana against vaccine-preventable diseases to equal or greater than 95%.
10. By 1992, increase the reported levels of fully immunized two year olds in Montana to equal or greater than 90%.
11. By 1992, develop a plan to assess immunization levels of persons in Montana at "high risk" for influenza and pneumococcal disease.

Other short-range objectives for the Montana Immunization Program include the areas of ensuring immunization in: health department employees; students attending colleges, universities, and vo-tech's; hospital employees; and family planning clients.

Other program activities include:

- a) Maintaining surveillance data on vaccine-preventable diseases;
- b) Responding to disease and suspected disease reports to control the spread and vaccinate susceptibles;
- c) Providing immunization education to health professionals and the general public;
- d) Maintaining inventory, storage, accounting and distribution of vaccine to public clinics;
- e) Establishing post-partum rubella vaccination policies in hospitals;
- f) Assisting hospitals in developing and implementing education for mothers of newborns;
- g) Reviewing clinics that provide program vaccine;
- h) Collecting immunization status information from schools and day cares;
- i) Assisting local health departments in implementing active disease surveillance systems;
- j) Visiting health care providers to assist in immunization service delivery;
- k) Ensuring graduating seniors have a standard immunization record;
- l) Conducting statewide promotional campaigns for immunization;
- m) Providing public education on the importance of immunization;
- n) Monitoring and reporting vaccine reactions;
- o) Developing systems to track females tested for rubella and determined to be susceptible;
- p) Establishing state term contracts for the purchase of vaccines not provided by the Program;
- q) Initiate immunization rule and law changes when necessary; and
- r) Ensuring all components of 1) the Immunization Program Announcement from the U.S.. Public Health Service and 2) the laws and rules of Montana that apply to immunization are followed.





## How to Use the Manual

Once completed, the Montana Immunization Manual will have five main subjects as described in the Table of Contents:

- I. Policy and Procedures -- Provides information on vaccines and records and contains references for vaccine-preventable diseases.
- II. Vaccine Contract -- You are to insert your signed copy of the current vaccine contract and a copy of the most recent clinic review.
- III. School/Day Care/College -- When completed, this will have copies of laws, rules, forms and instructions that relate to immunization requirements and recommendations in an educational setting in Montana.
- IV. Surveillance and Outbreak Control -- Will be a reference for identifying an outbreak and control of vaccine-preventable diseases.
- V. Promotional Materials and Order Forms -- Will display copies of Program forms, and samples and references for materials that can be used in promoting and educating about vaccines and vaccine-preventable diseases.

### Updating

The manual is being developed in loose leaf fashion for easy updating of individual pages or entire sections. The Montana Immunization Program will print and distribute current and updated information for use in the manual. The updates will include instructions as to what information is to be placed in, and what parts are to be removed from the manual. It is recommended that one person be responsible to see that the manual is kept up-to-date, immediately upon receiving new material.

### Log Sheet

In the front of the manual is an Update Log Sheet. Each time you receive information for the manual it should be noted on the log sheet with the date, description of the section that was updated, and initials of the person who updated the manual. Periodically you will receive a copy of the central office's log sheet which will reflect the entries that should be on your copy of the log sheet. The status of your copy of the manual will be assessed during visits by Immunization Program staff.

### Numbering of Pages

The table of contents (located in the front of the manual) includes separation of sections by tab number. Each "tab" section has its own table of contents by page number. All information included behind each tab is numbered sequentially.

### Goldenrod Colored Sections

Inserts that are copies of reference materials in the Policy and Procedures section are colored. They are numbered and correspond with related information.

Please feel free to call the Immunization Program office if there are any questions related to use of the manual.

DU NOT KEEP OUTDATED MATERIALS IN THIS MANUAL



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I. POLICY AND PROCEDURES

A. VACCINE SUPPLY

ORDERING VACCINE

1. When filling out the Vaccine Order Blank (HES-108)

- Use the complete name of your facility and name of contact person.
- Use your street address, and Box No. including zip code. UPS can not deliver to a post office box.
- In the column "No. of Doses" be sure to order by number of doses, not vials.

MONTANA IMMUNIZATION PROGRAM  
DEPARTMENT OF HEALTH AND ENVIRONMENTAL SCIENCES  
Cooswell Building  
Helena, Montana 59620

V A C C I N E O R D E R B L A N K

Listed below are the vaccines provided by the Immunization Program, State Department of Health. There is no charge for the vaccines, however you must pay for shipping containers and ice packs to be returned to the Program. Vaccines will be shipped early in the week to ensure delivery by the weekend. PLEASE ORDER A 90-DAY SUPPLY AT ONE TIME.

NEXT CLINIC DATE (if any) September 15

NOTE: Vaccine supplied by the Program must be accounted for on a monthly basis. Form HES-111(green), Vaccine Report Form, will be supplied for vaccine usage reporting. The report is due the 5th day of the month following the month being reported. Failure to comply could result in loss of "free" vaccine to your facility.

| <u>VACCINE REQUESTED</u>  | <u>NUMBER OF<br/>DOSES</u>                 | <u>CONSENT FORMS<br/>NEEDED</u> |
|---|--|---------------------------------|
| OPV (Oral Polio singles)  | <u>150</u>                                 | <u>none</u>                     |
| DTP (Diphtheria-Tetanus-Pertussis)<br>15-dose vials                 | <u>150</u>                                 | <u>150</u>                      |
| Hib (Haemophilus b Polysaccharide)<br>single-dose vials in box of 5 | <u>20</u>                                  | <u>20</u>                       |
| Td (Tetanus-Diphtheria - age 7 & up)<br>10-dose vials               | <u>20</u>                                  | <u>20</u>                       |
| MMR (Measles-Mumps-Rubella)<br>single-dose vials in box of 10       | <u>30</u>                                  | <u>50</u>                       |
| M-R (Measles-Rubella)<br>single-dose vials in box of 10             | <u>          </u>                          | <u>          </u>               |
| Diluent (used with MMR & M-R)                                       | <u>30</u>                                  | <u>          </u>               |
| Additional requests for supplies                                    | <u>200 Record and Signature cards: 250</u> |                                 |
| Official Immunization Record Cards:                                 | <u>10 Vaccine Report Forms</u>             |                                 |

Name Public Health Clinic \$15.00 will be charged  
Address Main Street your facility for NOT  
City Yourtown returning vaccine  
State MT shipping containers.  
Zip 59000 Return containers as  
Phone 555-0000 (Mary Smith, RN) soon as possible.

Shipping containers must be returned with the ice packs after each shipment.



2. Vaccine is shipped Monday and Tuesday only unless arrival-pickup can be assured for other days. Orders received after those days will be shipped the following week. Vaccine is not shipped in July-August, nor on days when the temperature is expected to exceed 80°F or below 10°F., due to lack of assurance of safe arrival.

NOTE: Vaccine orders placed within two weeks of when vaccine is needed, will not warrant special attention. Please plan ahead.

3. If Immunization Program staff have scheduled a visit to a vaccine provider, arrangements can be made for vaccine delivery to reduce shipping costs and ensure vaccine safety on delivery.
4. A call will be made to your office informing you of method and approximate time of delivery.
5. Arrangements must be made (by your office) for receipt and immediate storage of vaccine.
6. Sufficient vaccine should be ordered to have a two month supply on hand at all times. Do not order more vaccine than can be used in four months.
7. Loss of vaccine due to outdating has been an expensive problem. Vaccine providers who fail to follow the vaccine contract provision of notifying the Immunization Program 60 days in advanced of vaccine expiration dates will be responsible for the vaccine loss.
8. When your biologicals have been received be sure to:
  - Check the shipping container thoroughly to ensure all vaccine is removed.
  - Compare the vaccine received with your vaccine order. Sign the receipt line, enter the date and time vaccine was received, enter the condition in which the vaccine and container were when received, and return the yellow copy of the vaccine shipment receipt form (HES110) to the Immunization Program.
  - Keep the white copy for your records.
  - Refrigerate vaccines immediately.
  - If polio vaccine is still cold but in a liquid state, indicate on the box that one "freeze/thaw" occurred. It must be put in the freezer immediately upon receipt. (See Refrigeration Recommendation: Attachment of the Vaccine Contract).





- Place vaccines with the shortest outdate in an area of the refrigeration unit where they will be used first.
  - Return polyfoam container with cardboard mailer and ice packs to the Immunization Program. (There is a \$15.00 charge for unreturned polyfoam containers/cardboard mailers).
9. Vaccine may be picked up from the Immunization Program office from 8:00 a.m. through 4:30 p.m. Monday through Friday with a 24 hour notice. Room C303, Cogswell Building, 1400 Broadway, Helena, Montana (444-4740).

#### Borrowing, Returning and Shipping Vaccine

Due to our present inventory system, we cannot keep track of vaccine exchanged between clinics. We recommend the following guidelines if you find it is necessary to do so:

When borrowing vaccine from another clinic, you must replace the borrowed vaccine by requesting extra vaccine on your next vaccine order. Those loaning vaccine must continue to count the loaned vaccine as part of their inventory. Those borrowing vaccine should not count the borrowed vaccine as part of their inventory. We encourage you to maintain a sufficient vaccine inventory to avoid this procedure.

When sending vaccine to another clinic or returning unused vaccine to the Montana Immunization Program, use the following shipment procedures:

- 1) Always call the recipient to inform them of method of mailing and when vaccine should be expected to arrive.

- 2) To pack vaccine:

Use an insulated container and frozen ice packs. Pack polio vaccine directly against ice pack(s) and wrap together in paper. Place in container with ice pack on top. MMR/MR/- Measles vaccine can be packed directly against the ice.

DTP/Td, Hib vaccine and diluent should be packed at the top with paper or foam pellets in between the vaccine and the ice pack. Direct contact with the ice may cause vaccine to freeze.

- 3) Best methods of mailing are UPS, Priority Mail and Bus. Do not ship vaccine in extreme heat (80° or hotter) or cold (10° or colder). Ship on Monday and Tuesday only to avoid vaccine loss over a weekend.

Please remember, vaccine providers are responsible and accountable for vaccine shipped to and received from the Immunization Program.



### Storage, Handling and Temperature Monitoring

Recommendations for handling and storage of biologicals are provided on the chart entitled "VACCINE MANAGEMENT -- RECOMMENDATIONS FOR HANDLING AND STORAGE OF SELECTED BIOLOGICALS", which is attached to the Vaccine Contract exhibits (Section II). Additional copies are available from the Immunization Program on request.

Only authorized personnel should have access to the vaccine storage unit.

### Storage and Handling

Refer to STORAGE AND HANDLING section for individual recommendations for each vaccine.

In addition, when new vaccine arrives, make sure older vaccine is moved to the front of the refrigerator or freezer so that the vaccine with the shortest outdate material is used first. Also make a note on your Vaccine Report Form (HES-111) when you open a new lot number of vaccine.

DO NOT destroy vaccines that have reached temperatures beyond the recommended storage range. If you suspect that a vaccine has been rendered useless because of exposure to temperature extremes, label it accordingly and immediately place it in storage at the proper temperature. Consult with the Immunization Program before administering the vaccine or before returning it to the Immunization Program.

### Temperature Monitoring

In order to assure vaccine is maintained at proper storage temperatures, your freezer and refrigerator must have -- at the minimum -- accurate thermometer(s) and a temperature log sheet for daily recording (Monday thru Friday) and monitoring temperature(s). Any departure from normal temperature should be noted and corrective action taken immediately to restore optimal storage conditions. (Remember: Take precautions not to allow vaccine to exceed recommended temperatures). Ideally the vaccine storage refrigerator/freezer should be equipped with recording thermometers and alarms which sound when optimal storage temperatures are exceeded, and procedures established for response to alarms after hours. An inexpensive method for monitoring the freezer is an ice cube in a plastic cup or zip-lock bag. If the ice cube maintains its shape, it indicates freezer has maintained adequate temperature.

### Reporting Doses Used

The Monthly Vaccine Report Form is the method that each vaccine provider uses to report to the Montana Immunization Program information related to vaccine (i.e., doses on hand, doses administered, doses returned to the program, etc.). The data that is included in the report is consistent with the data that is required of the



program by CDC in order to continue receiving federally purchased vaccine. Requirements related to reporting vaccine usage are included in the Vaccine Contract. Instructions on filling out the report are attached. The following is an example of a properly completed Monthly Vaccine Report Form.

#### Destroying/Autoclaving Vaccine

Do not destroy or autoclave program vaccine unless directed to by the Immunization Program Manager. All outdated or damaged vaccine should be returned to the Montana Immunization Program for appropriate disposal if necessary. In the event that there has been a vaccine reaction or other situation in which the vaccine safety is questionable, contact the program for instructions on what to do with the vaccine in question. Any vaccine that is voluntarily destroyed by a vaccine provider, without seeking prior approval, will be counted as vaccine lost or wasted by the provider. The program performs surveillance for vaccine that may be unusable or unsafe. Upon receipt of a report of such vaccine the following will occur: 1) other state and national vaccine resources are notified of the situation to see if other similar situations have occurred, 2) CDC may be consulted to determine necessary action, and 3) the vaccine provider is notified as to what should happen with the vaccine in question.



# MONTHLY VACCINE REPORT FORM

(sample)

Name of Facility: Public Health Person Filing Report: Mary Smith, R.N.

Address: Main Street Report for the Month of: June Year: 88

City: Yourtown Zip: 59000 Phone Number of Reporting Facility: 555-0000

Zero Immunizations This Month \_\_\_\_\_

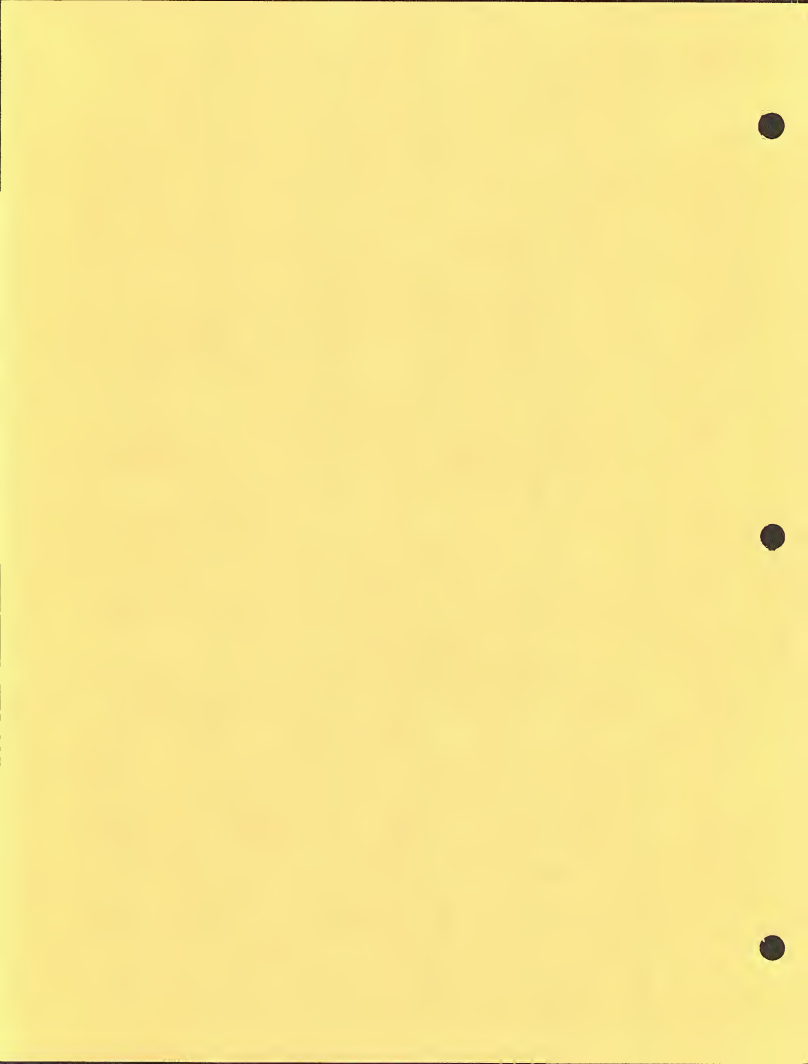
Vaccine Reactions (if checked, complete flip side) \_\_\_\_\_

More report forms needed \_\_\_\_\_

| Vaccine    | Doses On Hand Beg. Of Month | Doses Rec. During Month | Doses Returned To State | Total Doses Available | D O S E | Doses Administered By Age |     |     |      |      |      |       |       |       |       |       |      |      | Total Doses | Doses On Hand End of Month | Expiration Dates Of Vaccine On Hand |    |    |
|------------|-----------------------------|-------------------------|-------------------------|-----------------------|---------|---------------------------|-----|-----|------|------|------|-------|-------|-------|-------|-------|------|------|-------------|----------------------------|-------------------------------------|----|----|
|            |                             |                         |                         |                       |         | < 1                       | 1   | 2   | 3-4  | 5    | 6-9  | 10-14 | 15-19 | 20-24 | 25-44 | 45-64 | 65 + |      |             |                            |                                     |    |    |
| (1)        | (2)                         | (3)                     | (4)                     | (5)                   | (6)     | (7)                       | (8) | (9) | (10) | (11) | (12) | (13)  | (14)  | (15)  | (16)  | (17)  | (18) | (19) | (20)        | (21)                       |                                     |    |    |
| D.T.P.     | 52                          | 105                     |                         | 157                   | 1       | 5                         | 1   |     |      |      |      |       |       |       |       |       |      |      | 6           | 101                        | 5-2-89                              |    |    |
|            |                             |                         |                         |                       | 2       | 3                         | 1   |     |      |      |      |       |       |       |       |       |      |      |             |                            |                                     | 4  |    |
|            |                             |                         |                         |                       | 3       | 4                         | 2   |     |      |      |      |       |       |       |       |       |      |      |             |                            |                                     |    | 6  |
|            |                             |                         |                         |                       | 4+      |                           | 6   |     | 13   | 20   | 1    |       |       |       |       |       |      |      |             |                            |                                     |    | 40 |
|            |                             |                         |                         |                       | TOT     | 12                        | 10  |     | 13   | 20   | 1    |       |       |       |       |       |      |      |             |                            |                                     |    | 56 |
| Td (Adult) | 13                          | 0                       | 1lost (vial short)      | 12                    | 1       |                           |     |     |      |      |      |       |       |       |       |       |      |      |             | 7                          | 6-18-90                             |    |    |
|            |                             |                         |                         |                       | 2       |                           |     |     |      |      |      |       |       |       |       |       |      |      |             |                            |                                     |    |    |
|            |                             |                         |                         |                       | 3+      |                           |     |     |      |      |      |       |       | 2     | 3     |       |      |      |             |                            |                                     | 5  |    |
|            |                             |                         |                         |                       | TOT     |                           |     |     |      |      |      |       |       | 2     | 3     |       |      |      |             |                            |                                     | 5  |    |
| MI-R       | 0                           |                         |                         | 0                     |         |                           |     |     |      |      |      |       |       |       |       |       |      |      |             |                            |                                     |    |    |
| MI-M-R     | 24                          | 10                      |                         | 34                    |         |                           | 8   | 3   |      |      |      |       |       |       |       |       |      | 11   | 23          | 11-25-89                   |                                     |    |    |
| Oral Polio | 41                          | 150                     | 15 (exp)                | 176                   | 1       | 5                         | 1   |     |      |      |      |       |       |       |       |       |      |      | 6           | 118                        | 2-19-89                             |    |    |
|            |                             |                         |                         |                       | 2       | 3                         | 1   |     |      |      |      |       |       |       |       |       |      |      |             |                            |                                     | 4  |    |
|            |                             |                         |                         |                       | 3       | 4                         | 4   |     |      |      |      |       |       |       |       |       |      |      |             |                            |                                     | 8  |    |
|            |                             |                         |                         |                       | 4+      |                           | 6   |     | 13   | 20   | 1    |       |       |       |       |       |      |      |             |                            |                                     | 40 |    |
|            |                             |                         |                         |                       | TOT     | 12                        | 12  |     | 13   | 20   | 1    |       |       |       |       |       |      |      |             |                            |                                     | 58 |    |
| Tub        | 20                          | 0                       |                         | 20                    | 1       |                           |     | 5   | 3    |      |      |       |       |       |       |       |      |      | 8           | 12                         | 4-12-89                             |    |    |
|            |                             |                         |                         |                       | 2+      |                           |     |     |      |      |      |       |       |       |       |       |      |      |             |                            |                                     |    |    |
|            |                             |                         |                         |                       | TOT     |                           |     |     | 5    | 3    |      |       |       |       |       |       |      |      | 8           |                            |                                     |    |    |
| DT         | private purchase            |                         |                         |                       |         |                           | 2   | 1   |      |      |      |       |       |       |       |       |      | 3    | n/a         | 10-2-89                    |                                     |    |    |

Please read the instruction sheet before completing. Due by the fifth of each month (January report due by Feb. 5, etc.). If you have any questions please call 444-4740.

MONTANA DEPARTMENT OF HEALTH AND ENVIRONMENTAL SCIENCES, Immunization Program, Cogswell Building, Helena, MT 59620





Drug Company Information

The following is a list of drug manufacturers who produce and/or sell vaccine. Each company may vary in the types of vaccines that they produce and/or sell.

They also may frequently start and discontinue vaccine production. It is important to compare prices, types of vaccines, syringe availability, return policies, minimum orders, "quantity order" price breaks, etc. There are often vaccine promotional/educational materials also available when buying vaccines directly from the drug manufacturers.

Connaught Laboratories, Inc.  
Swiftwater, PA 18370

800-822-2463

Sclavo  
5 Mainsard Court  
Wayne, NJ 97470

800-526-5260

Lederle Laboratories  
Division of American Cynamid Co.  
One Cynamid Plaza  
Wayne, NJ 07470

800-533-3753

E.R. Squibb & Sons, Inc.  
P.O. Box 4000  
Princeton, NJ 98543-4000

800-241-5364

Merck, Sharp & Dohme  
Division of Merck & Co., Inc.  
West Point, PA 19486

800-<sup>992</sup>~~922~~-2929

Up-John Company  
7000 Portage Road  
Kalamazoo, MI 49001

616-323-4000

Merieux Institute  
P.O. Box 523980  
Miami, FL 33152

800-327-2842

Wyeth  
Division of American  
Home Products Corp.  
P.O. Box 8299  
Philadelphia, PA 19101

215-688-4400

Miles Inc. Cutter Biological  
400 Morgan Lane  
West Haven, CT 06516

800-227-1762

Parke-Davis  
Division of Warner-Lambert  
201 Tabor Road  
Morris Plains, NJ 07950  
800-223-0432



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B. IMMUNIZATION CLINIC SITE CONSIDERATIONS

It is best to have a controlled setting for an immunization clinic. In the event that it is necessary to have an immunization clinic away from the normal setting (i.e., school clinic, mass clinic, home visits, etc.) the risks and the benefits need to be considered. If such an immunization setting is necessary, each provider must have a written procedure in place to cover the situation. Consider the following areas in making the decision to proceed with the immunizations:

1. Disease potential (i.e., if there is a measles outbreak, a school immunization clinic may be necessary).
2. Patient non-compliance. Could they come to the regular immunization clinic?
3. Availability to provide emergency procedures. Is there a physician and medical facility available should an emergency occur? Is there an E.R. tray that's ready and available for use?
4. Vaccine quality. Can you ensure that the vaccine will be maintained properly?
5. Liability.
6. Meeting requirements of the Vaccine Contract.



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C. RECORD RETENTION AND MANAGEMENT

The Federal government mandates that the following applies to vaccines received through federal grants:

Important Information Statements must be retained for a period of ten years following the end of the calendar year in which the form is signed. In addition, if a notice of a claim or law suit has been made, the Important Information Statement pertaining to the matter should be retained until after the final disposition of the claim or litigation (including appeals). In certain situations, the government may need to rely upon the absence of an Important Information Statement as evidence that a vaccine was not administered; consequently, it is essential that you be able to show that a form or copy of the form has been retained for the 10-year period for each vaccination administered.

Microfilm copies of the forms may also be used as long as you keep a record of the procedures followed and can testify as to the uniform, invariable practice of microfilming all forms of this nature in a given locality and interval of time. The procedures followed must be adequate to allow administration of the forms or microfilm copies under either of the following Federal Rules of Evidence:

1. Rule 803(6). Records of regularly conducted activity. This rule allows the admission into evidence of records which are made as a memorandum of an act if:
  - a) It was made at or near the time of the event;
  - b) It was made in the course of a regularly conducted business activity;
  - c) It was customary to make the type of entry involved; and
  - d) It was within the personal knowledge of the entrant or within the knowledge of someone with the duty to transmit such matters to the entrant.
2. Rule 803(8). Public records and reports. This rule makes admissible records of public officials or agencies setting forth the activities of the office or agency, or matters observed pursuant to a legal duty to report, or factual findings resulting from an investigation in civil actions.

Evidence must be available that the criteria established under these rules are satisfied for each form, as to the form's original use and the procedure used in microfilming the form.

The Montana Immunization Program recommends that no immunization records be destroyed or thrown away. Retention of Important Information Forms should follow the federal guidelines. However, history has shown us that often times, the only record that can be retrieved to document a persons immunization history is the record kept by the clinic (public or private)



where the immunization was given. These documents are of extreme importance when faced with disease outbreaks and school entry requirements. In the event that you feel the need to purge the original copy of an immunization record, please contact the Montana Immunization Program before taking action.

Records management can often be a problem. It may be useful to keep an "active" and an "inactive" file for persons receiving immunizations in your clinic. This will allow you, 1) the ability to identify the success of your clinic in immunization children on schedule (i.e., identify all children under two years of age that use your clinic and determine their compliance with the immunization schedule); and 2) freedom from sorting through old files to find a patients record.

The Montana Department of Administration (MDA) has developed a Records Management Policies and Procedures Manual that may be of value to clinics that want to develop a new system or "clean up" their old. It is comprehensive and applies to all record management systems. If you are interested in obtaining a copy, contact the Records Management Section (MDA) 444-2716.

The vaccine contract includes requirements related to retention of Important Information Forms and use of the Clinic Record and Signature Card.



such material only for the purpose of evaluating matters of medical care, therapy, and treatment for research and statistical purposes. Neither such in-hospital medical staff committee nor the members, agents, or employees thereof shall disclose the name or identity of any patient whose records have been studied in any report or publication of findings and conclusions of such committee, but such in-hospital medical staff committee, its members, agents, or employees shall protect the identity of any patient whose condition or treatment has been studied and shall not disclose or reveal the name of any such in-hospital patient.

History: En. Sec. 2, Ch. 104, L. 1969; R.C.M. 1947, 69-6302.

**50-16-205. Data confidential — inadmissible in judicial proceedings.** All data shall be confidential and shall not be admissible in evidence in any judicial proceeding, but this section shall not affect the admissibility in evidence of records dealing with the patient's hospital care and treatment.

History: En. Sec. 3, Ch. 104, L. 1969; R.C.M. 1947, 69-6303.

**Cross-References**

Montana Rules of Evidence, Title 26, ch. 10.

### Part 3

#### Confidentiality of Health Care Information

(Repealed. Sec. 31, Ch. 632, L. 1987)

**Part Compiler's Comments**

*Histories of Repealed Sections:*

50-16-301. En. Sec. 1, Ch. 578, L. 1979.

50-16-302. En. Sec. 2, Ch. 578, L. 1979.

50-16-303. En. Sec. 6, Ch. 578, L. 1979.

50-16-304. En. Sec. 8, Ch. 578, L. 1979.

50-16-305. En. Sec. 7, Ch. 578, L. 1979.

50-16-306 through 50-16-310 reserved.

50-16-311. En. Sec. 3, Ch. 578, L. 1979;

amd. Sec. 1, Ch. 725, L. 1985.

50-16-312. En. Sec. 4, Ch. 578, L. 1979.

50-16-313. En. Sec. 4, Ch. 578, L. 1979.

50-16-314. En. Sec. 5, Ch. 578, L. 1979.

### Part 4

#### Health Information Center

**50-16-401. Repealed. Sec. 1, Ch. 66, L. 1987.**

History: En. Sec. 1, Ch. 628, L. 1983.

### Part 5

#### Uniform Health Care Information

**Part Cross-References**

Right of privacy guaranteed, Art. II, sec. 10,  
Mont. Const.

**50-16-501. Short title.** This part may be cited as the "Uniform Health Care Information Act".

History: En. Sec. 1, Ch. 632, L. 1987.



**50-16-502. Legislative findings.** The legislature finds that:

(1) health care information is personal and sensitive information that if improperly used or released may do significant harm to a patient's interests in privacy and health care or other interests;

(2) patients need access to their own health care information as a matter of fairness, to enable them to make informed decisions about their health care and to correct inaccurate or incomplete information about themselves;

(3) in order to retain the full trust and confidence of patients, health care providers have an interest in assuring that health care information is not improperly disclosed and in having clear and certain rules for the disclosure of health care information;

(4) persons other than health care providers obtain, use, and disclose health record information in many different contexts and for many different purposes. It is the public policy of this state that a patient's interest in the proper use and disclosure of his health care information survives even when the information is held by persons other than health care providers.

(5) the movement of patients and their health care information across state lines, access to and exchange of health care information from automated data banks, and the emergence of multistate health care providers creates a compelling need for uniform law, rules, and procedures governing the use and disclosure of health care information.

History: En. Sec. 2, Ch. 632, L. 1987.

**50-16-503. Uniformity of application and construction.** This part must be applied and construed to effectuate their general purpose to make uniform the laws with respect to the treatment of health care information among states enacting them.

History: En. Sec. 3, Ch. 632, L. 1987.

**50-16-504. Definitions.** As used in this part, unless the context indicates otherwise, the following definitions apply:

(1) "Audit" means an assessment, evaluation, determination, or investigation of a health care provider by a person not employed by or affiliated with the provider, to determine compliance with:

- (a) statutory, regulatory, fiscal, medical, or scientific standards;
- (b) a private or public program of payments to a health care provider; or
- (c) requirements for licensing, accreditation, or certification.

(2) "Directory information" means information disclosing the presence and the general health condition of a patient who is an inpatient in a health care facility or who is receiving emergency health care in a health care facility.

(3) "General health condition" means the patient's health status described in terms of critical, poor, fair, good, excellent, or terms denoting similar conditions.

(4) "Health care" means any care, service, or procedure provided by a health care provider, including medical or psychological diagnosis, treatment, evaluation, advice, or other services that affect the structure or any function of the human body.

(5) "Health care facility" means a hospital, clinic, nursing home, laboratory, office, or similar place where a health care provider provides health care to patients.





(6) "Health care information" means any information, whether oral or recorded in any form or medium, that identifies or can readily be associated with the identity of a patient and relates to the patient's health care. The term includes any record of disclosures of health care information.

(7) "Health care provider" means a person who is licensed, certified, or otherwise authorized by the laws of this state to provide health care in the ordinary course of business or practice of a profession. The term does not include a person who provides health care solely through the sale or dispensing of drugs or medical devices.

(8) "Institutional review board" means a board, committee, or other group formally designated by an institution or authorized under federal or state law to review, approve the initiation of, or conduct periodic review of research programs to assure the protection of the rights and welfare of human research subjects.

(9) "Maintain", as related to health care information, means to hold, possess, preserve, retain, store, or control that information.

(10) "Patient" means an individual who receives or has received health care. The term includes a deceased individual who has received health care.

(11) "Peer review" means an evaluation of health care services by a committee of a state or local professional organization of health care providers or a committee of medical staff of a licensed health care facility. The committee must be:

(a) authorized by law to evaluate health care services; and

(b) governed by written bylaws approved by the governing board of the health care facility or an organization of health care providers.

(12) "Person" means an individual, corporation, business trust, estate, trust, partnership, association, joint venture, government, governmental subdivision or agency, or other legal or commercial entity.

History: En. Sec. 4, Ch. 632, L. 1987.

50-16-505 through 50-16-510 reserved.

**50-16-511. Duty to adopt security safeguards.** A health care provider shall effect reasonable safeguards for the security of all health care information it maintains.

History: En. Sec. 21, Ch. 632, L. 1987.

**50-16-512. Content and dissemination of notice.** (1) A health care provider who provides health care at a health care facility that the provider operates and who maintains a record of a patient's health care information shall create a notice of information practices, in substantially the following form:

#### NOTICE

"We keep a record of the health care services we provide for you. You may ask us to see and copy that record. You may also ask us to correct that record. We will not disclose your record to others unless you direct us to do so or unless the law authorizes or compels us to do so. You may see your record or get more information about it at ....."



(2) The health care provider shall post a copy of the notice of information practices in a conspicuous place in the health care facility and upon request provide patients or prospective patients with a copy of the notice.

History: En. Sec. 18, Ch. 632, L. 1987.

**50-16-513. Retention of record.** A health care provider shall maintain a record of existing health care information for at least 1 year following receipt of an authorization to disclose that health care information under 50-16-526 and during the pendency of a request for examination and copying under 50-16-541 or a request for correction or amendment under 50-16-543.

History: En. Sec. 22, Ch. 632, L. 1987.

**50-16-514 through 50-16-520 reserved.**

**50-16-521. Health care representatives.** (1) A person authorized to consent to health care for another may exercise the rights of that person under this part to the extent necessary to effectuate the terms or purposes of the grant of authority. If the patient is a minor and is authorized under 41-1-402 to consent to health care without parental consent, only the minor may exclusively exercise the rights of a patient under this part as to information pertaining to health care to which the minor lawfully consented.

(2) A person authorized to act for a patient shall act in good faith to represent the best interests of the patient.

History: En. Sec. 19, Ch. 632, L. 1987.

**50-16-522. Representative of deceased patient.** A personal representative of a deceased patient may exercise all of the deceased patient's rights under this part. If there is no personal representative or upon discharge of the personal representative, a deceased patient's rights under this part may be exercised by persons who are authorized by law to act for him.

History: En. Sec. 20, Ch. 632, L. 1987.

**50-16-523 and 50-16-524 reserved.**

**50-16-525. Disclosure by health care provider.** (1) Except as authorized in 50-16-529 and 50-16-530 or as otherwise specifically provided by law or the Montana Rules of Civil Procedure, a health care provider, an individual who assists a health care provider in the delivery of health care, or an agent or employee of a health care provider may not disclose health care information about a patient to any other person without the patient's written authorization. A disclosure made under a patient's written authorization must conform to the authorization.

(2) A health care provider shall maintain, in conjunction with a patient's recorded health care information, a record of each person who has received or examined, in whole or in part, the recorded health care information during the preceding 3 years, except for an agent or employee of the health care provider or a person who has examined the recorded health care information under 50-16-529(2). The record of disclosure must include the name, address, and institutional affiliation, if any, of each person receiving or examining the recorded health care information, the date of the receipt or examination, and to the extent practicable a description of the information disclosed.

History: En. Sec. 5, Ch. 632, L. 1987.



**50-16-526. Patient authorization to health care provider for disclosure.** (1) A patient may authorize a health care provider to disclose the patient's health care information. A health care provider shall honor an authorization and, if requested, provide a copy of the recorded health care information unless the health care provider denies the patient access to health care information under 50-16-542.

(2) A health care provider may charge a reasonable fee, not to exceed his actual cost for providing the health care information, and is not required to honor an authorization until the fee is paid.

(3) To be valid, a disclosure authorization to a health care provider must:

- (a) be in writing, dated, and signed by the patient;
- (b) identify the nature of the information to be disclosed; and
- (c) identify the person to whom the information is to be disclosed.

(4) Except as provided by this part, the signing of an authorization by a patient is not a waiver of any rights a patient has under other statutes, the Montana Rules of Evidence, or common law.

History: En. Sec. 6, Ch. 632, L. 1987.

**50-16-527. Patient authorization — retention — effective period.**

(1) A health care provider shall retain each authorization or revocation in conjunction with any health care information from which disclosures are made.

(2) Except for authorizations to provide information to third-party health care payors, an authorization may not permit the release of health care information relating to health care that the patient receives more than 6 months after the authorization was signed.

(3) An authorization in effect on October 1, 1987, remains valid for 30 months after October 1, 1987, unless an earlier date is specified or it is revoked under 50-16-528. Health care information disclosed under such an authorization is otherwise subject to this part. An authorization written after October 1, 1987, becomes invalid after the expiration date contained in the authorization, which may not exceed 30 months. If the authorization does not contain an expiration date, it expires 6 months after it is signed.

History: En. Sec. 7, Ch. 632, L. 1987.

**50-16-528. Patient's revocation of authorization for disclosure.** A patient may revoke a disclosure authorization to a health care provider at any time unless disclosure is required to effectuate payments for health care that has been provided or other substantial action has been taken in reliance on the authorization. A patient may not maintain an action against the health care provider for disclosures made in good-faith reliance on an authorization if the health care provider had no notice of the revocation of the authorization.

History: En. Sec. 8, Ch. 632, L. 1987.

**50-16-529. Disclosure without patient's authorization based on need to know.** A health care provider may disclose health care information about a patient without the patient's authorization, to the extent a recipient needs to know the information, if the disclosure is:

- (1) to a person who is providing health care to the patient;



(2) to any other person who requires health care information for health care education; to provide planning, quality assurance, peer review, or administrative, legal, financial, or actuarial services to the health care provider; or for assisting the health care provider in the delivery of health care and if the health care provider reasonably believes that the person will:

(a) not use or disclose the health care information for any other purpose; and

(b) take appropriate steps to protect the health care information;

(3) to any other health care provider who has previously provided health care to the patient, to the extent necessary to provide health care to the patient, unless the patient has instructed the health care provider not to make the disclosure;

(4) to immediate family members of the patient or any other individual with whom the patient is known to have a close personal relationship, if made in accordance with the laws of the state and good medical or other professional practice, unless the patient has instructed the health care provider not to make the disclosure;

(5) to a health care provider who is the successor in interest to the health care provider maintaining the health care information;

(6) for use in a research project that an institutional review board has determined:

(a) is of sufficient importance to outweigh the intrusion into the privacy of the patient that would result from the disclosure;

(b) is impracticable without the use or disclosure of the health care information in individually identifiable form;

(c) contains reasonable safeguards to protect the information from improper disclosure;

(d) contains reasonable safeguards to protect against directly or indirectly identifying any patient in any report of the research project; and

(e) contains procedures to remove or destroy at the earliest opportunity, consistent with the purposes of the project, information that would enable the patient to be identified, unless an institutional review board authorizes retention of identifying information for purposes of another research project;

(7) to a person who obtains information for purposes of an audit, if that person agrees in writing to:

(a) remove or destroy, at the earliest opportunity consistent with the purpose of the audit, information that would enable the patient to be identified; and

(b) not disclose the information further, except to accomplish the audit or to report unlawful or improper conduct involving fraud in payment for health care by a health care provider or patient or other unlawful conduct by a health care provider; and

(8) to an official of a penal or other custodial institution in which the patient is detained.

History: En. Sec. 9, Ch. 632, L. 1987.

**Cross-References**

Duty of mental health professionals to warn of violent patients, 27-1-1102.

Nonliability for peer review, 37-2-201.

Pharmacists not liable for peer review, 37-7-1101.





**50-16-530. Disclosure without patient's authorization — other bases.** A health care provider may disclose health care information about a patient without the patient's authorization if the disclosure is:

(1) directory information, unless the patient has instructed the health care provider not to make the disclosure;

(2) to federal, state, or local public health authorities, to the extent the health care provider is required by law to report health care information or when needed to protect the public health;

(3) to federal, state, or local law enforcement authorities to the extent required by law;

(4) to a law enforcement officer about the general physical condition of a patient being treated in a health care facility if the patient was injured on a public roadway or was injured by the possible criminal act of another; or

(5) pursuant to compulsory process in accordance with 50-16-535 and 50-16-536.

History: En. Sec. 10, Ch. 632, L. 1987.

**50-16-531 through 50-16-534 reserved.**

**50-16-535. When health care information available by compulsory process.** Health care information may not be disclosed by a health care provider pursuant to compulsory legal process or discovery in any judicial, legislative, or administrative proceeding unless:

(1) the patient has consented in writing to the release of the health care information in response to compulsory process or a discovery request;

(2) the patient has waived the right to claim confidentiality for the health care information sought;

(3) the patient is a party to the proceeding and has placed his physical or mental condition in issue;

(4) the patient's physical or mental condition is relevant to the execution or witnessing of a will or other document;

(5) the physical or mental condition of a deceased patient is placed in issue by any person claiming or defending through or as a beneficiary of the patient;

(6) a patient's health care information is to be used in the patient's commitment proceeding;

(7) the health care information is for use in any law enforcement proceeding or investigation in which a health care provider is the subject or a party, except that health care information so obtained may not be used in any proceeding against the patient unless the matter relates to payment for his health care or unless authorized under subsection (9);

(8) the health care information is relevant to a proceeding brought under 50-16-551 through 50-16-553; or

(9) a court has determined that particular health care information is subject to compulsory legal process or discovery because the party seeking the information has demonstrated that there is a compelling state interest that outweighs the patient's privacy interest.

History: En. Sec. 11, Ch. 632, L. 1987.

**50-16-536. Method of compulsory process.** (1) Unless the court for good cause shown determines that the notification should be waived or modified, if health care information is sought under 50-16-535(2), (4), or (5) or in



a civil proceeding or investigation under 50-16-535(9), the person seeking discovery or compulsory process shall mail a notice by first-class mail to the patient or the patient's attorney of record of the compulsory process or discovery request at least 10 days before presenting the certificate required under subsection (2) to the health care provider.

(2) Service of compulsory process or discovery requests upon a health care provider must be accompanied by a written certification, signed by the person seeking to obtain health care information or his authorized representative, identifying at least one subsection of 50-16-535 under which compulsory process or discovery is being sought. The certification must also state, in the case of information sought under 50-16-535(2), (4), or (5) or in a civil proceeding under 50-16-535(9), that the requirements of subsection (1) for notice have been met. A person may sign the certification only if the person reasonably believes that the subsection of 50-16-535 identified in the certification provides an appropriate basis for the use of discovery or compulsory process. Unless otherwise ordered by the court, the health care provider shall maintain a copy of the process and the written certification as a permanent part of the patient's health care information.

(3) Production of health care information under 50-16-535 and this section does not in itself constitute a waiver of any privilege, objection, or defense existing under other law or rule of evidence or procedure.

History: En. Sec. 12, Ch. 632, L. 1987.

**50-16-537 through 50-16-540 reserved.**

**50-16-541. Requirements and procedures for patient's examination and copying.** (1) Upon receipt of a written request from a patient to examine or copy all or part of his recorded health care information, a health care provider, as promptly as required under the circumstances but no later than 10 days after receiving the request, shall:

(a) make the information available to the patient for examination during regular business hours or provide a copy, if requested, to the patient;

(b) inform the patient if the information does not exist or cannot be found;

(c) if the health care provider does not maintain a record of the information, inform the patient and provide the name and address, if known, of the health care provider who maintains the record;

(d) if the information is in use or unusual circumstances have delayed handling the request, inform the patient and specify in writing the reasons for the delay and the earliest date, not later than 21 days after receiving the request, when the information will be available for examination or copying or when the request will be otherwise disposed of; or

(e) deny the request in whole or in part under 50-16-542 and inform the patient.

(2) Upon request, the health care provider shall provide an explanation of any code or abbreviation used in the health care information. If a record of the particular health care information requested is not maintained by the health care provider in the requested form, he is not required to create a new record or reformulate an existing record to make the information available in the requested form. The health care provider may charge a reasonable fee, not



to exceed the health care provider's actual cost, for providing the health care information and is not required to permit examination or copying until the fee is paid.

History: En. Sec. 13, Ch. 632, L. 1987.

**50-16-542. Denial of examination and copying.** (1) A health care provider may deny access to health care information by a patient if the health care provider reasonably concludes that:

(a) knowledge of the health care information would be injurious to the health of the patient;

(b) knowledge of the health care information could reasonably be expected to lead to the patient's identification of an individual who provided the information in confidence and under circumstances in which confidentiality was appropriate;

(c) knowledge of the health care information could reasonably be expected to cause danger to the life or safety of any individual;

(d) the health care information was compiled and is used solely for litigation, quality assurance, peer review, or administrative purposes;

(e) the health care provider obtained the information from a person other than the patient; or

(f) access to the health care information is otherwise prohibited by law.

(2) Except as provided in 50-16-521, a health care provider may deny access to health care information by a patient who is a minor if:

(a) the patient is committed to a mental health facility; or

(b) the patient's parents or guardian have not authorized the health care provider to disclose the patient's health care information.

(3) If a health care provider denies a request for examination and copying under this section, the provider, to the extent possible, shall segregate health care information for which access has been denied under subsection (1) from information for which access cannot be denied and permit the patient to examine or copy the disclosable information.

(4) If a health care provider denies a patient's request for examination and copying, in whole or in part, under subsection (1)(a) or (1)(c), he shall permit examination and copying of the record by another health care provider who is providing health care services to the patient for the same condition as the health care provider denying the request. The health care provider denying the request shall inform the patient of the patient's right to select another health care provider under this subsection.

History: En. Sec. 14, Ch. 632, L. 1987.

**50-16-543. Request for correction or amendment.** (1) For purposes of accuracy or completeness, a patient may request in writing that a health care provider correct or amend its record of the patient's health care information to which he has access under 50-16-541.

(2) As promptly as required under the circumstances but no later than 10 days after receiving a request from a patient to correct or amend its record of the patient's health care information, the health care provider shall:

(a) make the requested correction or amendment and inform the patient of the action and of the patient's right to have the correction or amendment sent to previous recipients of the health care information in question;



(b) inform the patient if the record no longer exists or cannot be found;  
(c) if the health care provider does not maintain the record, inform the patient and provide him with the name and address, if known, of the person who maintains the record;

(d) if the record is in use or unusual circumstances have delayed the handling of the correction or amendment request, inform the patient and specify in writing the earliest date, not later than 21 days after receiving the request, when the correction or amendment will be made or when the request will otherwise be disposed of; or

(e) inform the patient in writing of the provider's refusal to correct or amend the record as requested, the reason for the refusal, and the patient's right to add a statement of disagreement and to have that statement sent to previous recipients of the disputed health care information.

History: En. Sec. 15, Ch. 632, L. 1987.

**50-16-544. Procedure for adding correction, amendment, or statement of disagreement.** (1) In making a correction or amendment, the health care provider shall:

(a) add the amending information as a part of the health record; and

(b) mark the challenged entries as corrected or amended entries and indicate the place in the record where the corrected or amended information is located, in a manner practicable under the circumstances.

(2) If the health care provider maintaining the record of the patient's health care information refuses to make the patient's proposed correction or amendment, the provider shall:

(a) permit the patient to file as a part of the record of his health care information a concise statement of the correction or amendment requested and the reasons therefor; and

(b) mark the challenged entry to indicate that the patient claims the entry is inaccurate or incomplete and indicate the place in the record where the statement of disagreement is located, in a manner practicable under the circumstances.

History: En. Sec. 16, Ch. 632, L. 1987.

**50-16-545. Dissemination of corrected or amended information or statement of disagreement.** (1) A health care provider, upon request of a patient, shall take reasonable steps to provide copies of corrected or amended information or of a statement of disagreement to all persons designated by the patient and identified in the health care information as having examined or received copies of the information sought to be corrected or amended.

(2) A health care provider may charge the patient a reasonable fee, not exceeding the provider's actual cost, for distributing corrected or amended information or the statement of disagreement, unless the provider's error necessitated the correction or amendment.

History: En. Sec. 17, Ch. 632, L. 1987.

**50-16-546 through 50-16-550 reserved.**

**50-16-551. Criminal penalty.** (1) A person who by means of bribery, theft, or misrepresentation of identity, purpose of use, or entitlement to the





information examines or obtains, in violation of this part, health care information maintained by a health care provider is guilty of a misdemeanor and upon conviction is punishable by a fine not exceeding \$10,000 or imprisonment for a period not exceeding 1 year, or both.

(2) A person who, knowing that a certification under 50-16-536(2) or a disclosure authorization under 50-16-526 and 50-16-527 is false, purposely presents the certification or disclosure authorization to a health care provider is guilty of a misdemeanor and upon conviction is punishable by a fine not exceeding \$10,000 or imprisonment for a period not exceeding 1 year, or both.

History: En. Sec. 23, Ch. 632, L. 1987.

**50-16-552. Civil enforcement.** The attorney general or appropriate county attorney may maintain a civil action to enforce this part. The court may order any relief authorized by 50-16-553.

History: En. Sec. 24, Ch. 632, L. 1987.

**50-16-553. Civil remedies.** (1) A person aggrieved by a violation of this part may maintain an action for relief as provided in this section.

(2) The court may order the health care provider or other person to comply with this part and may order any other appropriate relief.

(3) A health care provider who relies in good faith upon a certification pursuant to 50-16-536(2) is not liable for disclosures made in reliance on that certification.

(4) No disciplinary or punitive action may be taken against a health care provider or his employee or agent who brings evidence of a violation of this part to the attention of the patient or an appropriate authority.

(5) In an action by a patient alleging that health care information was improperly withheld under 50-16-541 and 50-16-542, the burden of proof is on the health care provider to establish that the information was properly withheld.

(6) If the court determines that there is a violation of this part, the aggrieved person is entitled to recover damages for pecuniary losses sustained as a result of the violation and, in addition, if the violation results from willful or grossly negligent conduct, the aggrieved person may recover not in excess of \$5,000, exclusive of any pecuniary loss.

(7) If a plaintiff prevails, the court may assess reasonable attorney fees and all other expenses reasonably incurred in the litigation.

(8) An action under this part is barred unless the action is commenced within 3 years after the cause of action accrues.

History: En. Sec. 25, Ch. 632, L. 1987.

## CHAPTER 17

### TUBERCULOSIS CONTROL

#### Part 1 — General Provisions

50-17-101. Policy of state.

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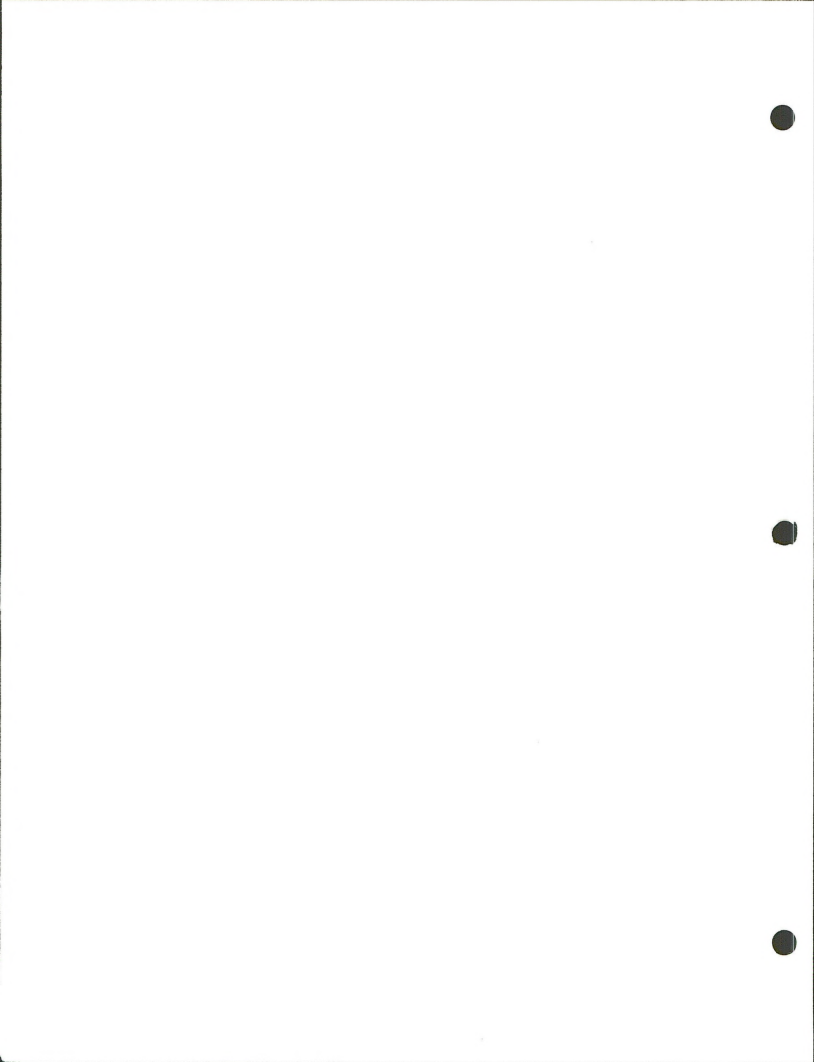
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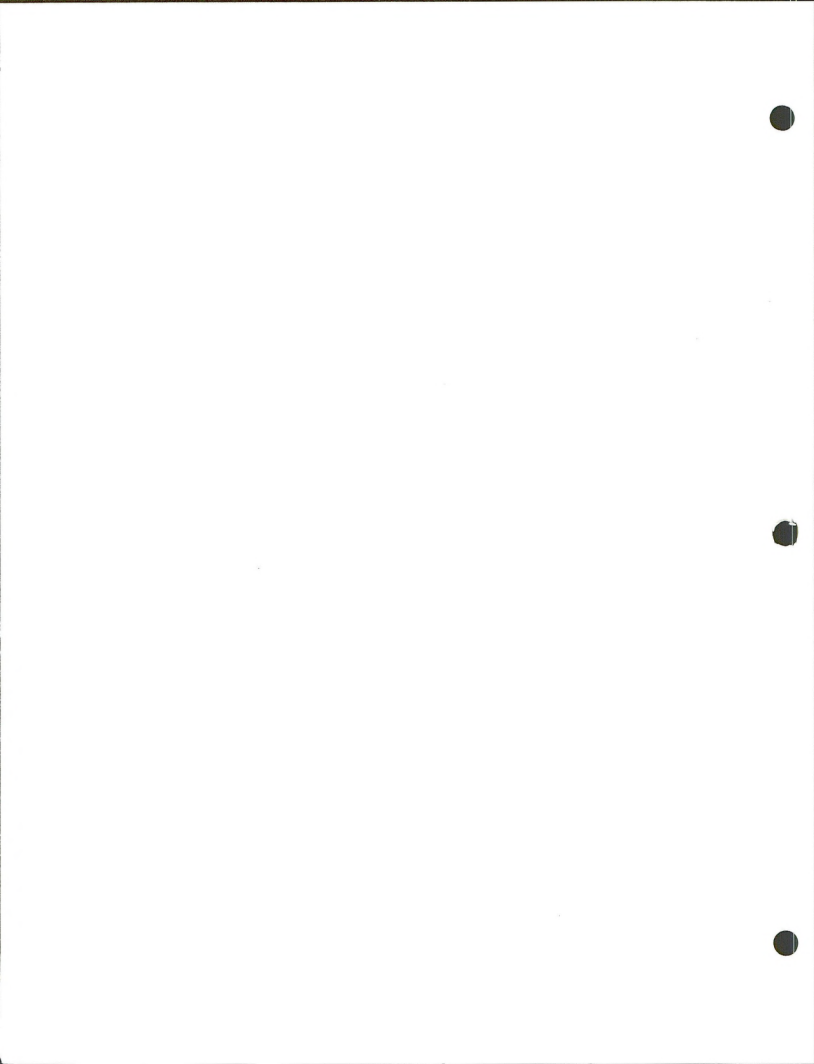




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### Special Circumstances

Although the ACIP should be the first reference to use in determining immunization criteria, the following references may also be used for immunization in special circumstances or conditions.

| <u>Circumstance or Condition</u>                           | <u>Reference</u> |
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| Treatment for anaphylactic reactions                       | Red Book         |
| Preterm infants  | Red Book         |
| Pregnancy  | Red Book         |
|  | *ACOG            |
| Immunodeficient and immuno-compromised children            | Red Book         |
| Infected with HIV or AIDS<br>(see attached ACIP statement) |                  |
| Asplenic children  | Red Book         |
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| Active Immunization after exposure to disease              | Red Book         |
| Children in Residential Institutions                       | Red Book         |
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| Adolescents and College Populations                        | Red Book         |
| Health care Professionals                                  | Red Book         |
| Refugees   | Red Book         |
| Foreign Travel   | Red Book         |
| Children in Day Care                                       | Red Book         |
| Isolation precautions for hospitalized children            | Red Book         |

\*ACOG: The American College of Obstetricians and Gynecologists  
600 Maryland Avenue S.W.  
Washington, D.C. 20024-2588  
Phone: (202) 638-5577

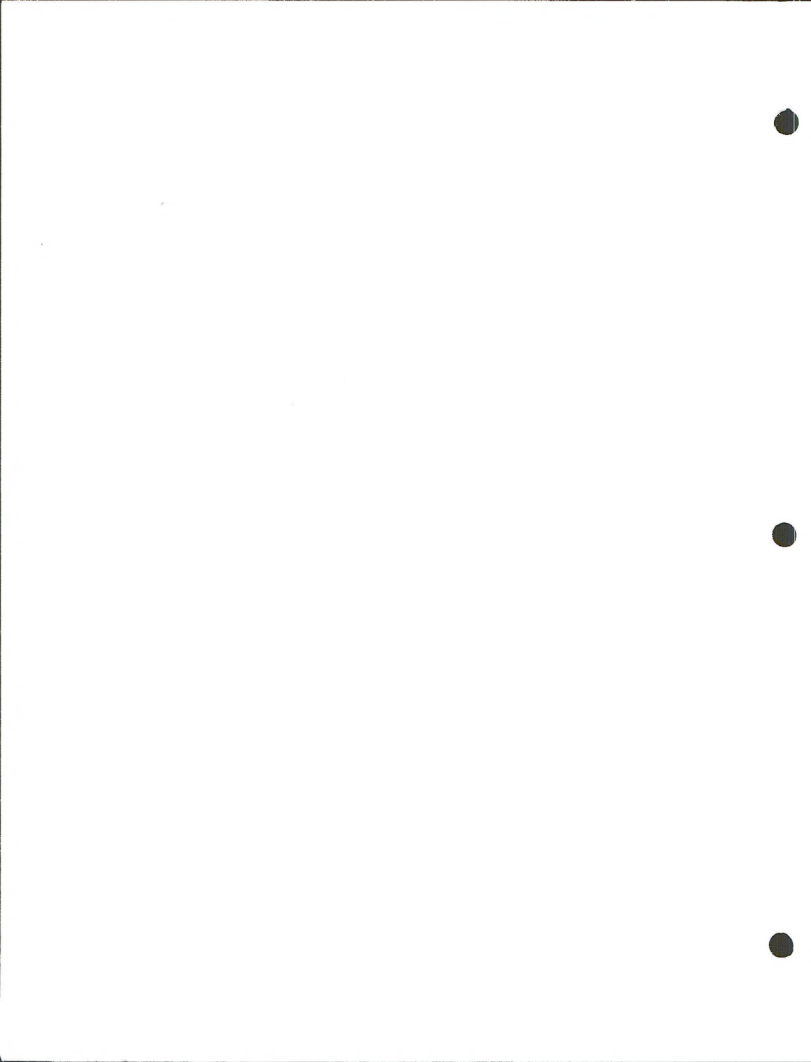
A copy of the ACOG Technical Bulletin - Immunization During Pregnancy follows.



ACOG

Section ~

Not RECEIVED  
Yet





Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**General Recommendations on Immunization**

*This revision of the "General Recommendations on Immunization" updates the 1983 statement (1). Changes or new sections include 1) listing of vaccines available in the United States by type and recommended routes, 2) updated schedules for immunizing infants and children, 3) clarification of the guidelines for spacing administration of immune globulin preparations and different vaccines, 4) an updated table of recommendations for routine immunization of children infected with human immunodeficiency virus, 5) listing of conditions that are often inappropriately considered contraindications to immunization, and 6) addition of information on the National Childhood Vaccine Injury Act of 1986 and the National Vaccine Injury Compensation Program. These recommendations are not comprehensive for each vaccine; Immunization Practices Advisory Committee (ACIP) recommendations on each vaccine should be consulted for more details.*

**INTRODUCTION**

Recommendations for immunizing infants, children, and adults are based on characteristics of immunobiologics, scientific knowledge about the principles of active and passive immunization, and judgments by public health officials and specialists in clinical and preventive medicine. Benefits and risks are associated with the use of all immunobiologics: no vaccine is completely safe or completely effective. Benefits of immunization range from partial to complete protection against the consequences of disease (which range from mild or asymptomatic infection to severe consequences, such as paralysis or death); risks of immunization range from common, trivial, and inconvenient side effects to rare, severe, and life-threatening conditions. Thus, recommendations for immunization practices balance scientific evidence of benefits, costs, and risks to achieve optimal levels of protection against infectious diseases. These recommendations describe this balance and attempt to minimize the risks by providing specific advice regarding dose, route, and spacing of immunobiologics and delineating situations that warrant precautions or contraindicate their use. They are recommendations for use in the United States because epidemiologic circumstances and vaccines often differ in other countries. Individual circumstances may warrant deviations from these recommendations. The relative balance of benefits and risks can change as diseases are controlled or eradicated. For example, because smallpox has been eradicated throughout the world, the risk of complications associated with smallpox vaccine now exceeds the risk of the disease; consequently, smallpox vaccination of civilians is now indicated only for laboratory workers directly involved with smallpox or closely related orthopox viruses (e.g., monkeypox and vaccinia).

**DEFINITIONS**

**Immunobiologic**

Immunobiologics include both antigenic substances, such as vaccines and toxoids, and antibody-containing preparations, including globulins and antitoxins, from human or animal donors. These products are used for active or passive immunization or therapy. Examples include:

**Vaccine (Table 1):** A suspension of live (usually attenuated) or inactivated microorganisms (bacteria, viruses, or rickettsiae) or fractions thereof administered to induce immunity and thereby prevent infectious disease. Some vaccines contain highly defined antigens (e.g., the polysaccharide of *Haemophilus influenzae* type b or the surface antigen of hepatitis B); others have antigens that are complex or incompletely defined (e.g., killed *Bordetella pertussis* or live attenuated viruses).

**Toxoid:** A modified bacterial toxin that has been rendered nontoxic but retains the ability to stimulate the formation of antitoxin.

**Immune globulin (IG):** A sterile solution containing antibodies from human blood. It is obtained by cold ethanol fractionation of large pools of blood plasma and contains 15%–18% protein. Intended for

**TABLE 1. Vaccines available in the United States, by type and recommended routes of administration**

| Vaccine  | Type   | Route   |
|--|--|---|
| BCG (Bacillus of Calmette and Guérin)  | Live bacteria  | Intradermal or subcutaneous                                 |
| Cholera  | Inactivated bacteria   | Subcutaneous or intradermal*                                |
| DTP<br>(D = Diphtheria)<br>(T = Tetanus)<br>(P = Pertussis)                  | Toxoids and inactivated bacteria                                 | Intramuscular   |
| HB (Hepatitis B)   | Inactive viral antigen   | Intramuscular   |
| Haemophilus influenzae b<br>- Polysaccharide (HbPV)<br>- or Conjugate (HbCV) | Bacterial polysaccharide or Polysaccharide conjugated to protein | Subcutaneous or intramuscular <sup>†</sup><br>Intramuscular |
| Influenza  | Inactivated virus or viral components                            | Intramuscular   |
| IPV (Inactivated Poliovirus Vaccine)   | Inactivated viruses of all 3 serotypes                           | Subcutaneous  |
| Measles  | Live virus   | Subcutaneous  |
| Meningococcal  | Bacterial polysaccharides of serotypes A/C/Y/W-135               | Subcutaneous  |
| MMR<br>(M = Measles)<br>(M = Mumps)<br>(R = Rubella)                         | Live viruses   | Subcutaneous  |
| Mumps  | Live virus   | Subcutaneous  |
| OPV (Oral Poliovirus Vaccine)  | Live viruses of all 3 serotypes                                  | Oral  |
| Plague   | Inactivated bacteria   | Intramuscular   |
| Pneumococcal   | Bacterial polysaccharides of 23 pneumococcal types               | Intramuscular or subcutaneous                               |
| Rabies   | Inactivated virus  | Subcutaneous or intradermal <sup>‡</sup>                    |
| Rubella  | Live virus   | Subcutaneous  |
| Tetanus  | Inactivated toxin (toxoid)                                       | Intramuscular <sup>†</sup>                                  |
| Td or DT**<br>(T = Tetanus)<br>(D or d = Diphtheria)                         | Inactivated toxins (toxoids)                                     | Intramuscular <sup>†</sup>                                  |
| Typhoid  | Inactivated bacteria   | Subcutaneous <sup>††</sup>                                  |
| Yellow fever   | Live virus   | Subcutaneous  |

\*The intradermal dose is lower.

<sup>†</sup>Route depends on the manufacturer; consult package insert for recommendation for specific product used.

<sup>‡</sup>Intradermal dose is lower and used only for preexposure vaccination.

<sup>††</sup>Preparations with adjuvants should be given intramuscularly.

\*\*DT = tetanus and diphtheria toxoids for use in children aged <7 years. Td = tetanus and diphtheria toxoids for use in persons aged ≥7 years. Td contains the same amount of tetanus toxoid as DTP or DT but a reduced dose of diphtheria toxoid.

<sup>†††</sup>Boosters may be given intradermally unless acetone-killed and dried vaccine is used.

intramuscular administration, it is primarily indicated for routine maintenance of immunity of certain immunodeficient persons and for passive immunization against measles and hepatitis A. IG does not transmit hepatitis B virus, human immunodeficiency virus (HIV), or other infectious diseases.

**Intravenous immune globulin (IGIV):** A product derived from blood plasma from a donor pool similar to the IG pool but prepared so it will be suitable for intravenous use. IGIV does not transmit infectious diseases. It is primarily indicated for replacement therapy in antibody-deficiency disorders.

**Specific IG:** Special preparations obtained from blood plasma from donor pools preselected for a high antibody content against a specific antigen, e.g., hepatitis B immune globulin (HBIG), varicella-zoster immune globulin, rabies immune globulin, and tetanus immune globulin. Like IG and IGIV, these preparations do not transmit infectious diseases.

**Antitoxin:** A solution of antibodies derived from the serum of animals immunized with specific antigens (e.g., diphtheria antitoxin, botulinum antitoxin) used to achieve passive immunity or for treatment.

### **Vaccination and Immunization**

These terms are often used interchangeably. *Vaccination* and *vaccine* derive from *vaccinia*, the virus once used as smallpox vaccine. Thus, *vaccination* originally meant inoculation with *vaccinia* virus to render a person immune to smallpox. Although some persons still prefer that *vaccination* be restricted to this use, most use it to denote the administration of any vaccine or toxoid.

*Immunization* is a more inclusive term denoting the process of inducing or providing immunity artificially by administering an immunobiologic. Immunization can be active or passive.

*Active immunization* is the production of antibody or other immune responses to the administration of a vaccine or toxoid. *Passive immunization* means the provision of temporary immunity by the administration of preformed antibodies. Three types of immunobiologics are administered for passive immunization: 1) pooled human IG or IGIV, 2) specific IG preparations, and 3) antitoxins.

*Vaccination* and *immunization* are used interchangeably in ACIP statements in reference to active immunization. Regardless of which term is used, administration of an immunobiologic cannot be automatically equated with the development of adequate immunity for a variety of reasons, many of which are discussed below.

### **IMMUNOBIOLOGICS**

The specific nature and content of immunobiologics can differ. When immunobiologics against the same infectious agents are produced by different manufacturers, active and inert ingredients in the various products are not always the same. Practitioners are urged to become familiar with the constituents of the products they use.

#### **Suspending Fluids**

These may be sterile water or saline or complex fluids containing small amounts of protein or other constituents derived from the medium or biologic system in which the vaccine is produced (e.g., serum proteins, egg antigens, cell-culture-derived antigens).

#### **Preservatives, Stabilizers, Antibiotics**

These components of vaccines, antitoxins, and globulins are used to inhibit or prevent bacterial growth in viral cultures or the final product or to stabilize the antigens or antibodies. Allergic reactions can occur if the recipient is sensitive to one of these additives (e.g., mercurials, phenols, albumin, glycine).

#### **Adjuvants**

Many antigens evoke insufficient immunologic responses when given in their natural state. Efforts to enhance immunogenicity include mixing antigens with a variety of substances or adjuvants (e.g., aluminum adjuvants such as aluminum phosphate).

### **ROUTE, SITE, AND TECHNIQUE OF IMMUNIZATION**

#### **Route**

Routes of administration are recommended for each immunobiologic (Table 1). To avoid unnecessary local or systemic effects and/or to ensure optimal efficacy, the practitioner should not deviate from the recommended routes. Vaccines containing adjuvants must be injected deep into the muscle mass; they should not be administered subcutaneously or intradermally because they can cause local irritation, inflammation, granuloma formation, or necrosis.

#### **Site**

Injectable immunobiologics should be administered where there is little likelihood of local, neural, vascular, or tissue injury. Subcutaneous injections are usually administered into the thigh of infants

and in the deltoid area of older children and adults. Intradermal injections are generally given on the volar surface of the forearm except for human diploid cell rabies vaccine with which reactions are less severe in the deltoid area. The preferred sites for intramuscular injections are the anterolateral aspect of the upper thigh and the deltoid muscle of the upper arm. In most infants, the anterolateral aspect of the thigh provides the largest muscle mass and is therefore the preferred site. An individual decision must be made for each child based on the volume of the material to be administered and the size of the muscle into which it is to be injected. In adults, the deltoid is recommended for routine intramuscular vaccine administration, particularly for hepatitis B vaccine. *The buttock should not be used routinely as a vaccination site for infants, children, or adults because of the risk of injury to the sciatic nerve.* In addition, injection into the buttock has been associated with decreased immunogenicity of hepatitis B and rabies vaccines, presumably because of inadvertent subcutaneous injection or injection into deep fat tissue. If the buttock is used when very large volumes are to be injected or multiple doses are necessary (e.g., large doses of iG), the central region should be avoided; only the upper, outer quadrant should be used.

#### **Techniques**

Syringes and needles used for injections must be sterile and preferably disposable to minimize the risk of contamination. For an intramuscular injection, the needle and syringe should be of sufficient length and bore to reach the muscle mass itself and prevent vaccine from seeping into subcutaneous tissue. For children, a 20- or 22-gauge needle 1 to 1¼ inches long is recommended. For small infants, a 25-gauge ¾-inch-long needle may be adequate. For adults, the suggested needle length is 1½ inches. For subcutaneous or intradermal injections, a 25-gauge needle ¾-¾ inches long is recommended.

Before the injection is given, the needle is inserted in the site and the syringe plunger pulled back; if blood appears, the needle should be withdrawn and a new site selected. The process should be repeated until no blood appears. A separate needle and syringe should be used for each vaccine injected. Disposable needles and syringes should be discarded into labeled, puncture-proof containers to prevent accidental needlesticks or reuse. If more than one vaccine preparation is administered or if vaccine and iG are administered simultaneously, each should be given at a different site.

#### **DOSAGE**

The recommendations on dosages of immunobiologics are derived from theoretical considerations, experimental trials, and clinical experience. Administration of volumes smaller than those recommended, such as split doses or intradermal administration (unless specifically recommended), can result in inadequate protection. Use of larger than the recommended dose can be hazardous because of excessive local or systemic concentrations of antigens.

The ACIP strongly discourages any variation from the recommended volume or number of doses of any vaccine. Some practitioners use smaller, divided, doses of vaccine, thereby reducing the total immunizing dose. Others use multiple smaller doses that together equal a full immunizing dose (e.g., diphtheria and tetanus toxoids and pertussis vaccine [DTP]) in an effort to reduce reactions. However, the serologic response, clinical efficacy, and/or frequency and severity of adverse reactions of such schedules have not been adequately studied.

#### **AGE AT WHICH IMMUNOBIOLOGICS ARE ADMINISTERED**

Several factors influence recommendations concerning the age at which vaccines are administered (Table 2); they are age-specific risks of disease, age-specific risks of complications, ability of persons of a given age to respond to the vaccine(s), and potential interference with the immune response by passively transferred maternal antibody. In general, vaccines are recommended for the youngest age group at risk whose members are known to develop an acceptable antibody response to vaccination.

#### **SPACING OF IMMUNOBIOLOGICS**

##### **Multiple Doses of Same Antigen**

Some products require administration of more than one dose for development of an adequate antibody response. In addition, some products require periodic reinforcement (booster) doses to maintain protection. In recommending the ages and/or intervals for multiple doses, the ACIP takes into account risks from disease and the need to induce or maintain satisfactory protection (Tables 2, 3, and 4).

Intervals between doses that are longer than those recommended do not lead to a reduction in final antibody levels. Therefore, it is not necessary to restart an interrupted series of an immunobiologic or to add extra doses.

In contrast, giving doses of a vaccine or toxoid at less than recommended intervals may lessen the antibody response and therefore should be avoided. Doses given at less than recommended intervals should not be counted as part of a primary series.

Some vaccines produce local or systemic symptoms in certain recipients when given too frequently (e.g., Td, DT, and rabies). Such reactions are thought to result from the formation of antigen-antibody complexes. Good recordkeeping, careful patient histories, and adherence to recommended schedules can decrease the incidence of such reactions without sacrificing immunity.

#### Different Antigens

Experimental evidence and extensive clinical experience have strengthened the scientific basis for giving certain vaccines at the same time. Many of the widely used vaccines can safely and effectively

**TABLE 2. Recommended schedule for active immunization of normal infants and children\***

| Recommended age <sup>1</sup> | Vaccine(s) <sup>2</sup>                    | Comments  |
|------------------------------|--|---|
| 2 mos                        | DTP#1 <sup>3</sup> , OPV#1 <sup>4</sup> ** | OPV and DTP can be given earlier in areas of high endemicity  |
| 4 mos                        | DTP#2, OPV#2                               | 6-wk to 2-mo interval desired between OPV doses   |
| 6 mos                        | DTP#3                                      | An additional dose of OPV at this time is optional in areas with a high risk of poliovirus exposure |
| 15 mos <sup>1†</sup>         | MMR <sup>5</sup> , DTP#4, OPV#3            | Completion of primary series of DTP and OPV   |
| 18 mos                       | HbCV <sup>6††</sup>                        | Conjugate preferred over polysaccharide vaccine***  |
| 4-6 yrs                      | DTP#5 <sup>1†††</sup> , OPV#4              | At or before school entry   |
| 14-16 yrs                    | Td <sup>5§§</sup>                          | Repeat every 10 yrs throughout life   |

\*See Table 3 for the recommended immunization schedules for infants and children up to their seventh birthday not immunized at the recommended times.

<sup>1</sup>These recommended ages should not be construed as absolute, e.g., 2 months can be 6-10 weeks. However, MMR should not be given to children <12 months of age. If exposure to measles disease is considered likely, then children 6 through 11 months old may be immunized with single-antigen measles vaccine. These children should be reimmunized with MMR when they are approximately 15 months of age.

<sup>2</sup>For all products used, consult the manufacturers' package enclosures for instructions regarding storage, handling, dosage, and administration. Immunobiologics prepared by different manufacturers can vary, and those of the same manufacturer can change from time to time. The package inserts are useful references for specific products, but they may not always be consistent with current ACIP and American Academy of Pediatrics immunization schedules.

<sup>3</sup>DTP = Diphtheria and Tetanus Toxoids and Pertussis Vaccine, Adsorbed. DTP may be used up to the seventh birthday. The first dose can be given at 6 weeks of age and the second and third doses given 4-8 weeks after the preceding dose.

<sup>4</sup>OPV = Poliovirus Vaccine Live Oral, Trivalent: contains poliovirus types 1, 2, and 3.

<sup>5</sup>Provided at least 6 months have elapsed since DTP#3 or, if fewer than 3 doses of DTP have been received, at least 6 weeks since the last previous dose of DTP or OPV. MMR vaccine should not be delayed to allow simultaneous administration with DTP and OPV. Administering MMR at 15 months and DTP#4 and OPV#3 at 18 months continues to be an acceptable alternative.

<sup>6</sup>MMR = Measles, Mumps, and Rubella Virus Vaccine, Live. Counties that report  $\geq 5$  cases of measles among preschool children during each of the last 5 years should implement a routine 2-dose measles vaccination schedule for preschoolers. The first dose should be administered at 9 months or the first health-care contact thereafter. Infants vaccinated before their first birthday should receive a second dose at about 15 months of age. Single-antigen measles vaccine should be used for children aged <1 year and MMR for children vaccinated on or after their first birthday. If resources do not allow a routine 2-dose schedule, an acceptable alternative is to lower the routine age for MMR vaccination to 12 months.

<sup>7</sup>HbCV = Vaccine composed of Haemophilus influenzae b polysaccharide antigen conjugated to a protein carrier. Children <5 years of age previously vaccinated with polysaccharide vaccine between the ages of 18 and 23 months should be revaccinated with a single dose of conjugate vaccine if at least 2 months have elapsed since the receipt of the polysaccharide vaccine.

<sup>8</sup>HbCV is not available, an acceptable alternative is to give Haemophilus influenzae b polysaccharide vaccine (HbPV) at age  $\geq 24$  months. Children at high risk for *Haemophilus influenzae* type b disease where conjugate vaccine is not available may be vaccinated with HbPV at 18 months of age and revaccinated at 24 months.

<sup>9</sup>Up to the seventh birthday.

<sup>§§</sup>Td = Tetanus and Diphtheria Toxoids, Adsorbed (for use in persons aged  $\geq 7$  years): contains the same amount of tetanus toxoid as DTP or DT but a reduced dose of diphtheria toxoid.

be given simultaneously (i.e., on the same day, *not* at the same site). This knowledge is particularly helpful when there is imminent exposure to several infectious diseases, preparation for foreign travel, or uncertainty that the person will return for further doses of vaccine.

### 1. Simultaneous administration

In general, inactivated vaccines can be administered simultaneously at separate sites. However, when vaccines commonly associated with local or systemic side effects (e.g., cholera, typhoid, and plague) are given simultaneously, the side effects can be accentuated. Whenever possible, these vaccines should be given on separate occasions.

Simultaneous administration of pneumococcal polysaccharide vaccine and whole-virus influenza vaccine elicits satisfactory antibody responses without increasing the incidence or severity of adverse reactions. Simultaneous administration of the pneumococcal vaccine and split-virus influenza vaccine can also be expected to yield satisfactory results. Influenza vaccine should be administered annually to the target population.

In general, simultaneous administration of the most widely used live and inactivated vaccines has not resulted in impaired antibody responses or increased rates of adverse reactions. Administration of combined measles, mumps, and rubella (MMR) vaccine yields results similar to administration of individual measles, mumps, and rubella vaccines at different sites. Therefore, there is no medical basis for giving these vaccines separately for routine immunization instead of the preferred MMR combined vaccine.

There are equivalent antibody responses and no clinically significant increases in the frequency of adverse events when DTP, MMR, and oral polio vaccine (OPV) or inactivated polio vaccine (IPV) are administered either simultaneously at different sites or separately. As a result, routine

**TABLE 3. Recommended immunization schedule for infants and children up to the seventh birthday not immunized at the recommended time in early infancy\***  
(See individual ACIP recommendations for details)

| Timing                            | Vaccine(s)  | Comments   |
|-----------------------------------|---|--|
| First visit                       | DTP#1 <sup>†</sup> , OPV#1 <sup>†</sup> ,<br>MMR <sup>‡</sup> if child is<br>aged ≥15 mos and<br>HbCV** if child is<br>aged ≥18 mos | DTP, OPV, and MMR should be administered simultaneously to children aged ≥15 mos, if appropriate. DTP, OPV, MMR, and HbCV may be given simultaneously to children aged 18 mos–5 yrs. |
| 2 mos after DTP#1,<br>OPV#1       | DTP#2 <sup>†</sup> , OPV#2  |  |
| 2 mos after DTP#2                 | DTP#3 <sup>††</sup>   | An additional dose of OPV at this time is optional in areas with a high risk of poliovirus exposure.   |
| 6–12 mos after DTP#3              | DTP#4, OPV#3  |  |
| Preschool <sup>§§</sup> (4–6 yrs) | DTP#5, OPV#4  | Preferably at or before school entry.  |
| 14–16 yrs                         | Td <sup>¶¶</sup>  | Repeat every 10 yrs throughout life.   |

\*If initiated in the first year of life, give DTP#1, 2, and 3 and OPV#1 and 2 according to this schedule; give MMR when the child becomes 15 months old.

<sup>†</sup>DTP = Diphtheria and Tetanus Toxoids and Pertussis Vaccine, Adsorbed. DTP can be used up to the seventh birthday.

<sup>††</sup>OPV = Poliovirus Vaccine Live Oral, Trivalent; contains poliovirus types 1, 2, and 3.

<sup>‡</sup>MMR = Measles, Mumps, and Rubella Virus Vaccine, Live (see text for discussion of single vaccines versus combination).

\*\*HbCV = Vaccine composed of Haemophilus influenzae b polysaccharide antigen conjugated to a protein carrier. If HbCV is not available, an acceptable alternative is to give Haemophilus influenzae b polysaccharide vaccine (HbPV) at 24 months of age. If HbCV is unavailable and if the child is at high risk for Haemophilus influenzae type b disease, HbPV may be given at 18 months of age with a second dose at 24 months. Children aged <5 years who were previously vaccinated with HbPV between 18 and 23 months of age should be revaccinated with a single dose of HbCV at least 2 months after the initial dose of HbPV. Either HbCV or HbPV can be administered up to the fifth birthday. However, they are not generally recommended for persons ≥5 years of age.

<sup>§§</sup>The second and third doses of DTP can be given 4–8 weeks after the preceding dose.

<sup>¶¶</sup>The preschool doses are not necessary if the fourth dose of DTP and third dose of OPV are administered after the fourth birthday.

<sup>¶¶¶</sup>Td = Tetanus and Diphtheria Toxoids, Adsorbed (for use in persons aged ≥7 years); contains the same dose of tetanus toxoid as DTP or DT and a reduced dose of diphtheria toxoid.

simultaneous administration of MMR, DTP, and OPV (or IPV) to all children  $\geq 15$  months who are eligible to receive these vaccines is recommended. Administration of MMR at 15 months followed by DTP and OPV (or IPV) at 18 months remains an acceptable alternative, especially for children with caregivers known to be generally compliant with other health-care recommendations. Data are lacking on concomitant administration of Haemophilus influenzae b conjugate vaccine (HbCV) or Haemophilus influenzae b polysaccharide vaccine (HbPV) and MMR and OPV vaccine. If the child might not be brought back for future immunizations, the simultaneous administration of all vaccines (including DTP, OPV, MMR, and HbCV or HbPV) appropriate to the age and previous vaccination status of the recipient is recommended. Hepatitis B vaccine given with DTP and OPV or given with yellow fever vaccine is as safe and efficacious as these vaccines administered separately.

The antibody responses of both cholera and yellow fever vaccines are decreased if given simultaneously or within a short time of each other. If possible, cholera and yellow fever vaccinations should be separated by at least 3 weeks. If there are time constraints and both vaccines are necessary, the injections can be given simultaneously or within a 3-week period with the understanding that antibody response may not be optimal. Decisions on the need for yellow fever and cholera immunizations should take into account the amount of protection afforded by the vaccine, the possibility that environmental or hygienic practices may be sufficient to avoid disease exposure, and the existence of vaccination requirements for entry into a country.

## 2. Nonsimultaneous administration

Inactivated vaccines do not interfere with the immune response to other inactivated vaccines or to live vaccines except, as noted above, with cholera and yellow fever vaccines. In general, an inactivated vaccine can be given either simultaneously or at any time before or after a different inactivated vaccine or a live vaccine.

There are theoretical concerns that the immune response to one live-virus vaccine might be impaired if given within 30 days of another. Whenever possible, live-virus vaccines not administered on the same day should be given at least 30 days apart (Table 5).

Live-virus vaccines can interfere with the response to a tuberculin test. Tuberculin testing can be done either on the same day that live-virus vaccines are administered or 4–6 weeks afterwards.

## Immune Globulin

If administration of an IG preparation becomes necessary because of imminent exposure to disease, live-virus vaccines can be given simultaneously with the IG product, with the recognition that

**TABLE 4. Recommended immunization schedule for persons  $\geq 7$  years of age not immunized at the recommended time in early infancy**  
(See individual ACIP recommendations for details)

| Timing                        | Vaccine(s)  | Comments   |
|-------------------------------|---|--|
| First visit                   | Td#1*, OPV#1 <sup>†</sup> ,<br>and MMR <sup>‡</sup> | OPV not routinely recommended for persons aged $\geq 18$ yrs |
| 2 mos after<br>Td#1, OPV#1    | Td#2, OPV#2   | OPV may be given as soon as 6 wks after OPV#1                |
| 6–12 mos after<br>Td#2, OPV#2 | Td#3, OPV#3   | OPV#3 may be given as soon as 6 wks after OPV#2              |
| 10 yrs after Td#3             | Td  | Repeat every 10 yrs throughout life                          |

\*Td = Tetanus and Diphtheria Toxoids, Adsorbed (For Adult Use) (for use after the seventh birthday). The DTP doses given to children  $< 7$  years who remain incompletely immunized at age  $\geq 7$  years should be counted as prior exposure to tetanus and diphtheria toxoids (e.g., a child who previously received 2 doses of DTP needs only 1 dose of Td to complete a primary series for tetanus and diphtheria).

<sup>†</sup>OPV = Poliovirus Vaccine Live Oral, Trivalent; contains poliovirus types 1, 2, and 3. When polio vaccine is to be given to persons  $\geq 18$  years, Poliovirus Vaccine Inactivated (IPV) is preferred. See ACIP statement on polio vaccine for immunization schedule for IPV (2).

<sup>‡</sup>MMR = Measles, Mumps, and Rubella Virus Vaccine, Live. Persons born before 1957 can generally be considered immune to measles and mumps and need not be immunized. Since medical personnel are at higher risk for acquiring measles than the general population, medical facilities may wish to consider requiring proof of measles immunity for employees born before 1957. Rubella vaccine can be given to persons of any age, particularly to nonpregnant women of childbearing age. MMR can be used since administration of vaccine to persons already immune is not deleterious (see text for discussion of single vaccines versus combination).

vaccine-induced immunity might be compromised. The vaccine should be administered at a site remote from that chosen for the IG inoculation. Vaccination should be repeated about 3 months later unless serologic testing indicates that specific antibodies have been produced. OPV and yellow fever vaccines are exceptions, however, and are not affected by administration of IG at any time.

Live, attenuated vaccine viruses might not replicate successfully, and antibody response could be diminished when the vaccine is given after IG or specific IG preparations. Whole blood or other antibody-containing blood products can interfere with the antibody response to measles, mumps, and rubella vaccines. In general, these parenterally administered live vaccines should not be given for at least 6 weeks, and preferably 3 months, after IG administration. However, the postpartum vaccination of susceptible women with rubella vaccine should not be delayed because of receipt of anti-Rho(D) IG (human) or any other blood product during the last trimester of pregnancy or at delivery. These women should be vaccinated immediately after delivery and, if possible, tested in 3 months to ensure that rubella immunity was established.

If administration of IG preparations becomes necessary after a live-virus vaccine has been given, interference can occur. Usually, vaccine virus replication and stimulation of immunity will occur 1–2 weeks after vaccination. Thus, if the interval between administration of live-virus vaccine and subsequent administration of an IG preparation is <14 days, vaccination should be repeated at least 3 months after the IG product was given, unless serologic testing indicates that antibodies were produced.

In general, there is little interaction between IG preparations and inactivated vaccines. Therefore, inactivated vaccines can be given simultaneously or at any time before or after an IG product is used. For example, postexposure prophylaxis with simultaneously administered hepatitis B, rabies, or tetanus IG and the corresponding inactivated vaccine or toxoid does not impair the immune response and provides immediate protection and long-lasting immunity. The vaccine and IG should be given at different sites, and standard doses of the corresponding vaccine should be used. Increasing the vaccine dose volume or number of immunizations is not indicated (Table 6).

#### HYPERSENSITIVITY TO VACCINE COMPONENTS

Vaccine components can cause allergic reactions in some recipients. These reactions can be local or systemic, including mild to severe anaphylaxis (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock). The responsible vaccine components can derive from: 1) animal protein, 2) antibiotics, 3) preservatives, and 4) stabilizers. The most common animal protein allergen is egg protein found in vaccines prepared using embryonated chicken eggs or chicken embryo cell cultures (e.g., yellow fever, mumps, measles, and influenza vaccines). Ordinarily, persons who are able to eat eggs or egg products safely can receive these vaccines; persons with histories of anaphylactic allergy to eggs or egg proteins should not.

Asking persons whether they can eat eggs without adverse effects is a reasonable way to screen for those who might be at risk from receiving measles, mumps, yellow fever, and influenza vaccines. Protocols requiring extreme caution have been developed for testing and vaccinating with measles and mumps vaccines those persons with anaphylactic reactions to egg ingestion (4). A regimen for administering influenza vaccine to children with egg hypersensitivity and severe asthma has also been developed (5).

**TABLE 5. Guidelines for spacing live and killed antigen administration**

| Antigen combination      | Recommended minimum interval between doses                           |
|--------------------------|--|
| >2 Killed antigens       | None. May be given simultaneously or at any interval between doses.* |
| Killed and live antigens | None. May be given simultaneously or at any interval between doses.† |
| >2 Live antigens         | 4-wk minimum interval if not administered simultaneously.            |

\*If possible, vaccines associated with local or systemic side effects (e.g., cholera, typhoid, plague vaccines) should be given on separate occasions to avoid accentuated reactions.

†Cholera vaccine with yellow fever vaccine is the exception. If time permits, these antigens should not be administered simultaneously, and at least 3 weeks should elapse between administration of yellow fever vaccine and cholera vaccine. If the vaccines must be given simultaneously or within 3 weeks of each other, the antibody response may not be optimal.



Rubella vaccine is grown in human diploid cell cultures and can safely be given to persons with histories of severe allergy to eggs or egg proteins.

Some vaccines contain trace amounts of antibiotics to which patients may be hypersensitive. The information provided in the vaccine package insert should be carefully reviewed before a decision is made whether the rare patient with such hypersensitivity should be given the vaccine(s). No currently recommended vaccine contains penicillin or its derivatives.

MMR and its individual component vaccines contain trace amounts of neomycin. Although the amount present is less than would usually be used for the skin test to determine hypersensitivity, persons who have experienced anaphylactic reactions to neomycin should not be given these vaccines. Most often, neomycin allergy is a contact dermatitis, a manifestation of a delayed-type (cell-mediated) immune response rather than anaphylaxis. A history of delayed-type reactions to neomycin is not a contraindication for these vaccines.

Bacterial vaccines, such as cholera, DTP, plague, and typhoid, are frequently associated with local or systemic adverse effects, such as redness, soreness, and fever. These reactions are difficult to link with a specific sensitivity to vaccine components and appear to be toxic rather than hypersensitive. On rare occasions, urticarial or anaphylactic reactions in DTP, DT, or Td recipients have been reported. When such events are reported, appropriate skin tests should be performed to determine sensitivity to tetanus toxoid before its use is discontinued (6).

#### ALTERED IMMUNOCOMPETENCE

Virus replication after administration of live, attenuated-virus vaccines can be enhanced in persons with immunodeficiency diseases and in persons with suppressed capacity for immune response as occurs with leukemia, lymphoma, generalized malignancy, symptomatic HIV infections, or therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids. Severe complications have followed vaccination with live, attenuated-virus vaccines and with live-bacteria vaccines (e.g., BCG) in patients with leukemia, lymphoma, or suppressed immune responses. In general, these patients should not be given live vaccines, with the exceptions noted below.

If polio immunization is indicated for immunosuppressed patients, their household members, or other close contacts, these persons should be given IPV rather than OPV. Although a protective immune response cannot be assured in the immunocompromised patient, some protection may be provided. Because of the possibility of immunodeficiency in other children born to a family in which one such case has occurred, no family members should receive OPV unless the immune statuses of the intended recipient and all other children in the family are known.

Patients with leukemia in remission whose chemotherapy has been terminated for at least 3 months can be given live-virus vaccines. Short-term, low-to-moderate dose systemic corticosteroid therapy (<2 weeks), topical steroid therapy (e.g., nasal, skin), long-term alternate-day treatment with low to

**TABLE 6. Guidelines for spacing the administration of immune globulin (IG) preparations and vaccines**

| Simultaneous administration:<br>Immunobiologic combination     |                | Recommended minimum interval between doses  |
|--|----------------|---|
| IG and killed antigen  |                | None. May be given simultaneously at different sites or at any time between doses.  |
| IG and live antigen  |                | Should generally not be given simultaneously.*<br>If unavoidable to do so, give at different sites and revaccinate or test for seroconversion in 3 mos. |
| Nonsimultaneous administration:<br>Immunobiologic administered |                | Recommended minimum interval between doses  |
| First  | Second         |   |
| IG   | Killed antigen | None  |
| Killed antigen   | IG             | None  |
| IG   | Live antigen   | 6 wks and preferably 3 mos*   |
| Live antigen   | IG             | 2 wks   |

\*The live-virus vaccines, oral polio and yellow fever, are exceptions to these recommendations. Either vaccine may be administered simultaneously or at any time before or after IG without significantly decreasing the antibody response (3).

moderate doses of short-acting systemic steroids, and intra-articular, bursal, or tendon injection with corticosteroids are not immunosuppressive in their usual doses and do not contraindicate live-virus vaccine administration.

The growing number of infants and preschoolers infected with HIV has directed special attention to the appropriate immunization of such children. The evaluation and testing for HIV infection of asymptomatic children presenting for vaccines is not necessary before decisions concerning immunization are made. The inactivated childhood vaccines (e.g., DTP or HbCV) should be given to HIV-infected children regardless of whether HIV symptoms are present. Although OPV has not been harmful when administered to asymptomatic HIV-infected children, IPV is the vaccine of choice if the child is known to be infected. The use of IPV not only eliminates any theoretical risk to the vaccinee but also prevents the possibility of vaccine virus spread to immunocompromised close contacts. Asymptomatically infected persons in need of MMR should receive it. Also, MMR should be considered for all symptomatic HIV-infected children since measles disease can be severe in symptomatic HIV-infected children. Limited studies of MMR immunization in both asymptomatic and symptomatic HIV-infected patients have not documented serious or unusual adverse events. In addition, pneumococcal vaccine is recommended for any child infected with HIV. Influenza vaccine is recommended for children with symptoms of HIV infection (Table 7).

#### FEBRILE ILLNESS

The decision to administer or delay vaccination because of a current or recent febrile illness depends largely on the severity of symptoms and on the etiology of the disease.

Although a moderate or severe febrile illness is reason to postpone immunizations, minor illnesses such as mild upper-respiratory infections (URI) with or without low-grade fever are not contraindications for vaccination. In persons whose compliance with medical care cannot be assured, it is particularly important to take every opportunity to provide appropriate vaccinations.

Children with moderate or severe febrile illnesses can be vaccinated as soon as the child has recovered. This precaution to wait avoids superimposing adverse effects of the vaccine on the underlying illness or mistakenly attributing a manifestation of the underlying illness to the vaccine.

Routine physical examinations or measuring temperatures are not prerequisites for vaccinating infants and children who appear to be in good health. Asking the parent or guardian if the child is ill, postponing vaccination in those with moderate or severe febrile illnesses, and immunizing those without contraindications to vaccination are appropriate procedures in childhood immunization programs.

#### VACCINATION DURING PREGNANCY

Because of a theoretical risk to the developing fetus, pregnant women or women likely to become pregnant within 3 months after vaccination should not be given live, attenuated-virus vaccines. With some of these vaccines—particularly rubella, measles, and mumps—pregnancy is a contraindication. Both yellow fever vaccine and OPV, however, can be given to pregnant women who are at substantial risk of exposure to natural infection. When a vaccine is to be given during pregnancy, waiting until the

TABLE 7. Recommendations for routine immunization of HIV-infected children — United States

| Vaccine      | Known HIV infection |             |
|--------------|---------------------|-------------|
|              | Asymptomatic        | Symptomatic |
| DTP*         | Yes                 | Yes         |
| OPV†         | No                  | No          |
| IPV‡         | Yes                 | Yes         |
| MMR§         | Yes                 | Yes**       |
| HbCV††       | Yes                 | Yes         |
| ¶neumococcal | Yes                 | Yes         |
| Influenza    | No§§                | Yes         |

\*DTP = Diphtheria and Tetanus Toxoids and Pertussis Vaccine, Adsorbed. DTP may be used up to the seventh birthday.

†OPV = Poliovirus Vaccine Live Oral, Trivalent; contains poliovirus types 1, 2, and 3.

‡IPV = Poliovirus Vaccine Inactivated; contains poliovirus types 1, 2, and 3.

§MMR = Measles, Mumps, and Rubella Virus Vaccine, Live.

\*\*Should be considered.

††HbCV = Vaccine composed of Haemophilus influenzae b polysaccharide antigen conjugated to a protein carrier.

§§Not contraindicated.

second or third trimester is a reasonable precaution to minimize concern over teratogenicity. Although there are theoretical risks, there is no evidence of congenital rubella syndrome in infants born to susceptible mothers who inadvertently were given rubella vaccine during pregnancy.

Persons given measles, mumps, or rubella vaccines can shed but not transmit these viruses. These vaccines can be administered safely to the children of pregnant women. Although live polio virus is shed by persons recently immunized with OPV (particularly after the first dose), this vaccine can also be administered to the children of pregnant women because experience has not revealed any risk of polio vaccine virus to the fetus.

There is no convincing evidence of risk to the fetus from immunizing the pregnant woman with inactivated virus or bacteria vaccines or toxoids. Previously immunized pregnant women who have not received a Td immunization within the last 10 years should receive a booster dose once past the first trimester. Women who are unimmunized or only partially immunized against tetanus should complete as much of the primary series as possible during the last two trimesters of the pregnancy. Depending on when the woman seeks prenatal care and the required interval between doses, one or two doses of Td can be administered before delivery. Eligible women who do not complete the required three-dose series during pregnancy should be followed after delivery to assure they receive the doses necessary for protection.

All pregnant women should be evaluated for immunity to rubella. Women susceptible to rubella should be immunized immediately after delivery. In addition, a woman's status as a carrier of hepatitis B should also be assessed during pregnancy. A woman infected with hepatitis B virus should be followed carefully so that her child can receive HBIG and the hepatitis B vaccine series shortly after delivery.

There is no known risk to the fetus from passive immunization of pregnant women with IG. Further information regarding immunization of pregnant women is available in the American College of Obstetricians and Gynecologists Technical Bulletin Number 64, May 1982.

#### MISCONCEPTIONS CONCERNING CONTRAINDICATIONS TO VACCINATION

Some health-care providers inappropriately consider certain conditions or circumstances contraindications to vaccination. Conditions most often *inappropriately* regarded as routine contraindications include the following:

1. Reaction to a previous dose of DTP vaccine that involved only soreness, redness, or swelling in the immediate vicinity of the vaccination site or temperature of  $<105\text{ F}$  ( $40.5\text{ C}$ ).
2. Mild acute illness with low-grade fever or mild diarrheal illness in an otherwise well child.
3. Current antimicrobial therapy or the convalescent phase of illnesses.
4. Prematurity. The appropriate age for initiating immunizations in the prematurely born infant is the usual chronologic age. Vaccine doses should not be reduced for preterm infants.
5. Pregnancy of mother or other household contact.
6. Recent exposure to an infectious disease.
7. Breastfeeding. The only vaccine virus that has been isolated from breast milk is rubella vaccine virus. There is no good evidence that breast milk from women immunized against rubella is harmful to infants.
8. A history of nonspecific allergies or relatives with allergies.
9. Allergies to penicillin or any other antibiotic, except anaphylactic reactions to neomycin (e.g., MMR-containing vaccines) or streptomycin (e.g., OPV). None of the vaccines licensed in the United States contain penicillin.
10. Allergies to duck meat or duck feathers. No vaccine available in the United States is produced in substrates containing duck antigens.
11. Family history of convulsions in persons considered for pertussis or measles vaccination (7,8).
12. Family history of sudden infant death syndrome in children considered for DTP vaccination.
13. Family history of an adverse event, unrelated to immunosuppression, following vaccination.

#### ADVERSE EVENTS FOLLOWING VACCINATION

Modern vaccines are safe and effective but not completely so. Adverse events have been reported following the administration of all vaccines. These events range from frequent, minor, local reactions to extremely rare, severe, systemic illness, such as paralysis associated with OPV. It is often impossible to establish evidence for cause-and-effect relationships when untoward events occur after vaccination because temporal association alone does not necessarily indicate causation. More complete information on adverse reactions to a specific vaccine may be found in the ACIP recommendations for each vaccine.

The National Vaccine Injury Compensation Program established by the National Childhood Vaccine Injury Act of 1986 requires physicians and other health-care providers who administer vaccines to maintain permanent immunization records and to report occurrences of certain adverse events to the U.S. Department of Health and Human Services. Recording and reporting requirements took effect on March 21, 1988. Reportable reactions include those listed in the Act for each vaccine (9,10) and events specified in the manufacturer's vaccine package insert as contraindications to further doses of that vaccine.

Although there will be one system for reporting adverse events following immunizations in the future, at present there are two separate systems. The appropriate method depends on the source of funding used to purchase the vaccine. Events that occur after receipt of a vaccine purchased with public (federal, state, and/or local government) funds must be reported by the administering health provider to the appropriate local, county, or state health department. The state health department completes and submits the correct forms to CDC. Reportable events that follow administration of vaccines purchased with private money are reported by the health-care provider directly to the Food and Drug Administration (FDA).

#### PATIENT INFORMATION

Parents, the responsible caregiver, or adult patients should be informed about the benefits and risks of vaccine in understandable language. Ample opportunity for questions and answers should be provided before each immunization. CDC has developed "Important Information Statements" for use with federally purchased vaccines given in public health clinics, but similar statements have not been universally adopted for the private medical-care sector.

An Important Information Statement must be developed for each vaccine covered by the National Childhood Vaccine Injury Act (DTP or component antigens, MMR or component antigens, IPV, and OPV). These statements are to be used by *all public and private* providers of vaccines. Until the Important Information Statements established by the Act become available, the current CDC Important Information Statements should be used in public health clinics and other settings where publicly purchased vaccines are used. The use of similar statements in the private sector is encouraged.

#### VACCINE PROGRAMS

The best way to reduce vaccine-preventable diseases is to have a highly immune population. Universal immunization is an important part of good health care and should be accomplished through routine and intensive programs carried out in physicians' offices and in public health clinics. Programs aimed at ensuring that all children are immunized at the recommended ages should be established and maintained in all communities. In addition, appropriate immunizations should be available for all adults.

Every visit to a health-care provider is an opportunity to update a patient's immunization status with needed vaccines. All adults should complete a primary series of tetanus and diphtheria toxoids, then receive a booster dose every 10 years. Persons  $\geq 65$  years old and all adults with medical conditions that place them at risk for pneumococcal disease or serious complications of influenza should receive one dose of pneumococcal polysaccharide vaccine and annual injections of influenza vaccine. In addition, immunization programs for adults should provide MMR vaccine whenever possible to anyone believed susceptible to measles, mumps, or rubella. Use of MMR ensures that the recipient has been immunized against three different diseases and causes no harm if the vaccinee is already immune to one or more of its components.

Official health agencies should take necessary steps, including developing and enforcing school immunization requirements, to assure that students at all grade levels, including college students, and those in child-care centers are protected against vaccine-preventable diseases. Agencies should also encourage institutions such as hospitals and extended-care facilities to adopt policies regarding the appropriate immunization of residents and employees.

Dates of immunization (day, month, and year) should be recorded on institutional immunization records, such as those kept in schools and child-care centers. This will facilitate assessments that a primary vaccine series has been completed according to an appropriate schedule and that needed boosters have been obtained at the correct time.

Tickler or recall systems can identify children who are due for immunizations or are behind schedule so parents can be contacted and reminded to have their children immunized. The ACIP recommends the use of these systems by all health-care providers. Such systems should also be developed by health-care providers who treat adults to ensure that at-risk persons receive influenza vaccine annually.

## IMMUNIZATION RECORDS

Documentation of patient immunizations will help ensure that persons in need of vaccine receive it and that adequately vaccinated patients are not overimmunized with increased risk of hypersensitivity (e.g., tetanus toxoid hypersensitivity).

### Patient's Personal Record

Official immunization cards have been adopted by every state and the District of Columbia to encourage uniformity of records and to facilitate the assessment of immunization status by schools and child-care centers. The records are also important tools in immunization education programs aimed at increasing parental and patient awareness of the need for vaccines. A permanent immunization record card should be established for each newborn infant and maintained by the parent. In many states, these cards are distributed to new mothers before discharge from the hospital.

### Provider Records

The National Vaccine Injury Compensation Program requires each health-care provider to record in the vaccine recipient's permanent medical record (or in a permanent office log or file) the provider's name, address, and title (if appropriate), the type of immunobiologic administered, the manufacturer, lot number, and date of administration. *Health-care provider* is any licensed health-care professional, organization, or institution, whether private or public (including federal, state, and local departments and agencies), under whose authority a specified vaccine is administered. The vaccines covered under this new law include: DTP and MMR (or any of their components given singly or in combination), OPV, and IPV. A permanent immunization record should also be established and maintained for adults and children who receive vaccines not covered by the National Vaccine Injury Act. The ACIP recommends use of standard records that note the type, manufacturer, lot number, and date of administration for each immunobiologic administered. Serologic test results for vaccine-preventable diseases, such as those for rubella screening, as well as documented episodes of adverse events, should also be recorded in the vaccine recipient's permanent medical record.

### SOURCES OF VACCINE INFORMATION

In addition to these general recommendations, the practitioner can draw on a variety of sources for specific data and updated information including:

**Official vaccine package circulars.** Manufacturer-provided product-specific information approved by the FDA with each vaccine. Some of these materials are reproduced in the *Physician's Desk Reference (PDR)*.

**Morbidity and Mortality Weekly Report (MMWR).** Published weekly by CDC, *MMWR* contains regular and special ACIP recommendations on vaccine use and statements of vaccine policy as they are developed and reports of specific disease activity. Subscriptions are available through Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402. Also available through MMS Publications, C.S.P.O. Box 9120, Waltham, MA 02254.

**Health Information for International Travel.** Booklet published annually by CDC as a guide to national requirements and with recommendations for specific immunizations and health practices for travel to foreign countries. Purchase from the Superintendent of Documents (address above).

**Advisory memoranda** are published as needed by CDC to advise international travelers or persons who provide information to travelers about specific outbreaks of communicable diseases abroad. They include health information for prevention and specific recommendations for immunization. Memoranda and/or placement on mailing list are available from Division of Quarantine, Center for Prevention Services (CPS), CDC, Atlanta, GA 30333.

**The Report of the Committee on Infectious Diseases** of the American Academy of Pediatrics (Red Book). This report, which contains recommendations on all licensed vaccines, is updated every 2-3 years, most recently in 1988. Policy changes for individual recommendations for immunization practices are published as needed by the American Academy of Pediatrics in the journal *Pediatrics*. They are available from American Academy of Pediatrics, Publications Division, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

**Control of Communicable Diseases in Man** is published by the American Public Health Association every 5 years, most recently in 1985 (14th ed.) The manual contains information about infectious diseases, their occurrence worldwide, diagnoses and therapy, and up-to-date recommendations on isolation and other control measures for each disease presented. It is available from the American Public Health Association, 1015 Fifteenth St. N.W., Washington, DC 20005.

*Guide for Adult Immunization (1985)* is produced by the American College of Physicians for physicians caring for adults. It emphasizes use of vaccines in healthy adults and adults with specific disease problems. It is available from American College of Physicians, Division of Scientific Activities, Health and Public Policy, 4200 Pine Street, Philadelphia, PA 19104.

Technical bulletins of the American College of Obstetricians and Gynecologists are updated periodically. These bulletins contain important information on immunization of pregnant women. They are available from American College of Obstetricians and Gynecologists, Attention: Resource Center, 409 12th Street S.W., Washington, DC 20024-2188.

State and many local health departments frequently provide technical advice, printed information on vaccines and immunization schedules, posters, and other educational materials.

Division of Immunization, CPS, CDC, Atlanta, GA 30333, telephone (404) 639-3311, offers technical advice on vaccine recommendations, disease outbreak control, and sources of immunobiologics. In addition, a course on the epidemiology, prevention, and control of vaccine preventable diseases is offered each year in Atlanta and, on occasion, in different states.

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Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**New Recommended Schedule  
for Active Immunization of Normal Infants and Children**

Until now, the recommended schedule for active immunization of normal infants and children called for administering combined measles-mumps-rubella (MMR) vaccine at 15 months and giving the fourth dose of Diphtheria and Tetanus Toxoids and Pertussis Vaccine (DTP) and the third dose of oral poliovirus vaccine (OPV) at 18 months (7). Two visits have been needed to receive these vaccines in the second year of life because the safety and efficacy of administering all three simultaneously had not been proven.\* A large, randomized, double-blind trial has recently been completed (2), and sufficient data are now available to recommend the simultaneous administration of MMR, DTP, and OPV to all children 15 months old or older who are eligible to receive these vaccines (Table 1).

In this trial, serologic response and clinical reaction rates following primary immunization with MMR were compared in a test group of 405 children given MMR simultaneously with DTP and OPV and a control group of 410 children given MMR followed by doses of DTP and OPV vaccine 2 months later. Seroconversion rates to each MMR component exceeded 96% in both groups, and the geometric mean titers achieved against the other six antigens were also similar in both groups. Rates of most of the common vaccine-associated clinical reactions to DTP and MMR were not augmented by simultaneous administration of these two vaccines. Some minor side effects were reported more frequently in the simultaneous-administration group; however, these differences were judged to be related to artifacts of the study design rather than to differences in the safety of the two vaccine schedules.

Data from CDC's Monitoring System for Adverse Events Following Immunization (MSAEFI) have been reviewed, particularly the information from Idaho, Louisiana, and Tennessee, where policies to administer MMR, DTP, and OPV simultaneously have been in effect for periods ranging from several months to years. Although there are limitations to the use of the MSAEFI data set for this purpose, the evidence suggests no increased risk of reactions associated with the simultaneous administration of these antigens.

Although the overall implications of simultaneous administration have not been fully defined, it is anticipated that implementation of this new schedule will result in at least three benefits: (1) a decrease in the number of health-care-provider visits required for immunization during the second year of life, (2) an accompanying decrease in costs, and (3) an increase in the percentage of children who will be fully or partially immunized by 24 months of age.

Some health-care providers may continue to prefer administering MMR at 15 months followed by DTP and OPV at 18 months, especially for patients who are known to be compliant with health-care recommendations or if other purposes are served by the additional visit. Such a schedule remains an acceptable alternative to the newly proposed schedule involving simultaneous administration of DTP, MMR, and OPV in a single visit.

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\*It should be noted that simultaneous administration of MMR, DTP, and OPV was previously recommended for children who were behind schedule in receiving their immunizations. This recommendation was based on the demonstrated safety and efficacy of other vaccine combinations (e.g., DTP and measles, or MMR and OPV).

TABLE 1. New recommended schedule for active immunization of normal infants and children\*

| Recommended age <sup>†</sup> | Vaccine(s) <sup>§</sup>         | Comments   |
|------------------------------|---------------------------------|--|
| 2 months                     | DTP-1 <sup>¶</sup> , OPV-1**    | Can be given earlier in areas of high endemicity.  |
| 4 months                     | DTP-2, OPV-2                    | 6-week to 2-month interval desired between OPV doses to avoid interference.  |
| 6 months                     | DTP-3                           | An additional dose of OPV at this time is optional for use in areas with a high risk of polio exposure.                                  |
| 15 months <sup>††</sup>      | MMR, <sup>§§</sup> DTP-4, OPV-3 | Completion of primary series of DTP and OPV.   |
| 24 months                    | HbPV <sup>¶¶</sup>              | Can be given at 18-23 months for children in groups who are thought to be at increased risk of disease, e.g., day-care-center attendees. |
| 4-6 years <sup>***</sup>     | DTP-5, OPV-4                    | Preferably at or before school entry.  |
| 14-16 years                  | Td <sup>†††</sup>               | Repeat every 10 years throughout life.   |

\*See Reference 1 for the recommended immunization schedules for infants and children up to their seventh birthday not immunized at the recommended time in early infancy and for persons 7 years of age or older.

<sup>†</sup>These recommended ages should not be construed as absolute, i.e., 2 months can be 6-10 weeks, etc.

<sup>§</sup>For all products used, consult manufacturer's package enclosure for instructions for storage, handling, and administration. Immunobiologics prepared by different manufacturers may vary, and those of the same manufacturer may change from time to time. The package insert should be followed for a specific product.

<sup>¶</sup>DTP-Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed.

\*\*OPV-Poliovirus Vaccine Live Oral; contains poliovirus strains Types 1, 2, and 3.

<sup>††</sup>Provided at least 6 months have elapsed since DTP-3 or, if fewer than three DTPs have been received, at least 6 weeks since last previous dose of DTP or OPV. MMR vaccine should not be delayed just to allow simultaneous administration with DTP and OPV. Administering MMR at 15 months and DTP-4 and OPV-3 at 18 months continues to be an acceptable alternative.

<sup>§§</sup>MMR-Measles, Mumps, and Rubella Virus Vaccine, Live.

<sup>¶¶</sup>Hemophilus b Polysaccharide Vaccine.

<sup>\*\*\*</sup>Up to the seventh birthday.

<sup>†††</sup>Td-Tetanus and Diphtheria Toxoids Adsorbed (For adult use)—contains the same dose of tetanus toxoid as DTP or DT and a reduced dose of diphtheria toxoid.



Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**Immunization of Children Infected with  
Human T-Lymphotropic Virus Type III/  
Lymphadenopathy-Associated Virus**

**INTRODUCTION**

This document is intended to summarize available information and to assist health-care providers in developing policies for the immunization of children infected with human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV),\* the virus that causes acquired immunodeficiency syndrome (AIDS). These policies may vary depending upon the prevalence of HTLV-III/LAV infection and the incidence of vaccine-preventable diseases in the community, individual assessment of a child's health status, and the risks and benefits of immunization in a particular situation. This discussion considers the risks and benefits of immunization for children residing in the United States based on the risks of vaccine-preventable diseases and the prevalence of HTLV-III/LAV infection and is intended for use by health-care providers in the United States. The recommendations may not pertain to other countries with different risks of vaccine-preventable diseases and prevalence of HTLV-III/LAV infection among children. Since these recommendations are based upon information and knowledge available at this time, periodic reassessment and revision will be required as more data concerning risk and benefits associated with immunization of HTLV-III/LAV-infected children become known and as the prevalences of specific vaccine-preventable diseases and HTLV-III infection change.

**HTLV-III/LAV INFECTION AMONG CHILDREN**

In the period June 1, 1981-September 2, 1986, physicians and health departments in the United States reported 24,430 cases of AIDS to CDC (7). Three hundred forty-five (1%) of the case-patients were children under 13 years of age who met the AIDS case definition; 75% of these pediatric cases were reported from New York, Florida, New Jersey, and California. Children with less severe manifestations of HTLV-III/LAV infection (AIDS-related complex, or ARC) or with asymptomatic infections are not now reported to CDC, and no seroprevalence studies have been conducted among children. Thus, the number of less severely affected children and the number of infected but presently asymptomatic children are uncertain. In one recently published case series, 14 (48%) of 29 symptomatic HTLV-III/LAV-infected children met the CDC criteria for AIDS (2).

Fifty percent of children reported to CDC were diagnosed as having AIDS during the first year of life; 82%, by 3 years of age (7). Sixty-five percent of pediatric AIDS cases reported to CDC were fatal (3). Short-term fatality rates are lower for children with less severe disease (ARC) who have not developed opportunistic infections; however, the ultimate prognosis of these children and of asymptomatic infected children is unknown.

**MECHANISMS OF TRANSMISSION OF HTLV-III/LAV AMONG CHILDREN**

Two risk factors are predominately associated with HTLV-III/LAV infection in children: a) being born to a mother who has HTLV-III/LAV infection, and b) receiving blood or clotting factors containing HTLV-III/LAV. Most case-patients (79%) are children whose mothers probably are infected with the virus. The major risk factors for infection of these women are intravenous (IV) drug abuse and sexual contact with men at risk of HTLV-III/LAV infection (primarily through drug abuse or bisexual contacts); women of Haitian or central African origin are also at a higher risk of acquiring HTLV-III/LAV infection, and a small percentage of infected women have a history of being transfused with blood (4). Approximately 15% of pediatric AIDS case-patients have received transfusions of blood or blood products, and 4% have hemophilia and have been treated with clotting-factor concentrates. Information about risk factors is incomplete for 3% of children with AIDS.

\*The AIDS virus has been variously termed human T-lymphotropic virus type III (HTLV-III/LAV), lymphadenopathy-associated virus (LAV), AIDS-associated retrovirus (ARV), or human immunodeficiency virus (HIV). The designation "human immunodeficiency virus" (HIV) has been accepted by a subcommittee of the International Committee for the Taxonomy of Viruses as the appropriate name for the retrovirus that has been implicated as the causative agent of AIDS (Science 1986;232:697)

Currently available data indicate that most pediatric HTLV-III/LAV infections are acquired from infected women during pregnancy, during labor and delivery, or perhaps shortly after birth. The risk of perinatal transmission from an infected mother to her infant is not known, although prospective studies indicate the rate of transmission has ranged from 0% (0/3) to 65% (13/20) (5-7). Seropositive women who had previously delivered an infected child had the highest of these transmission rates (65%) in subsequent pregnancies (5). In a retrospective study evaluating nine children whose mothers were later diagnosed as having AIDS, two (22%) children had antibody to HTLV-III/LAV (8). Additional prospective studies are needed to define more precisely the rate of perinatal transmission of HTLV-III/LAV.

#### PREVALENCE OF HTLV-III/LAV INFECTION AMONG WOMEN OF CHILD-BEARING AGE

The prevalence of HTLV-III/LAV infection among women of child-bearing age varies depending on the patient group and geographic area (4). Reported confirmed seroprevalences are less than 0.01% among female blood donors in Atlanta and 0.06% among female U.S. military recruit applicants (4,9). In contrast, the reported prevalence of HTLV-III/LAV antibody among IV drug abusers has ranged from 2% to 59%, with the highest prevalence in New York City and northern New Jersey. Female sex partners of IV drug-abusing men with AIDS or with ARC had a reported seroprevalence of 40%-71%, whereas 10% of female partners of asymptomatic infected hemophiliacs were reported to be seropositive (4). Seroprevalence among prostitutes has varied greatly (5%-40%) depending on the geographic area and has been largely attributed to a coincidental history of IV drug abuse (4). Seroprevalence has been reported to be as high as 5% among persons born in countries in which heterosexual transmission of HTLV-III/LAV is thought to play a major role (e.g., Haiti, central African countries) (1,10,11).

#### IMMUNOLOGIC ABNORMALITIES ASSOCIATED WITH HTLV-III/LAV INFECTION

Children with symptomatic HTLV-III/LAV infection (AIDS or ARC) have immunologic abnormalities similar to those of adult AIDS patients, including hypergammaglobulinemia, decreased T4 lymphocytes, reversed helper-suppressor T-cell ratios, poor T-lymphocyte responses to mitogen stimulation, and altered humoral immunity. Lymphopenia (cell counts less than 1,500 cells/mm<sup>3</sup>) is uncommon. Antibody responses of children with AIDS or ARC to diphtheria and tetanus toxoid boosters and to pneumococcal vaccine were absent or lower than those of age-matched controls, which is consistent with defective humoral immunity (12,13). Some HTLV-III/LAV-infected children responded adequately to immunization; 60% of AIDS and ARC patients given measles-mumps-rubella vaccine (MMR) prior to diagnosis had protective levels of measles antibodies 5-66 months after immunization (14).

Asymptomatic HTLV-III/LAV-infected adults as a group generally have less severe abnormalities of immunologic function than adults with AIDS or ARC, and some may have normal immunologic function, although individual asymptomatic adults may have severe abnormalities (15). Immunologic function of asymptomatic HTLV-III/LAV-infected children has not yet been adequately studied but presumably would be more intact than that of symptomatic HTLV-III/LAV-infected children. In a small prospective study, all 29 children with symptomatic HTLV-III/LAV infection had immunologic abnormalities within 5-13 months of being found infected, compared with only two of seven (29%) children reported to have asymptomatic HTLV-III/LAV infection (2).

#### CONCERNS ABOUT IMMUNIZATION OF HTLV-III/LAV-INFECTED CHILDREN

The immunologic abnormalities associated with symptomatic HTLV-III/LAV infection have raised concerns about the immunization of infected children. Replication of live, attenuated vaccine viruses may be enhanced in persons with immunodeficiency diseases and theoretically may produce serious adverse events following immunization of symptomatic HTLV-III/LAV-infected (AIDS and ARC) patients (16). Concerns have been expressed on theoretical grounds that antigenic stimulation by immunization with inactivated vaccines might lead to a deterioration of clinical status of HTLV-III/LAV-infected children, but this effect has not been documented (17). Since symptomatic HTLV-III/LAV-infected patients have abnormal primary and secondary antibody responses, the efficacy of immunization may be decreased (18). The efficacy of immunization for asymptomatic HTLV-III/LAV-infected children is unknown, but presumably would be higher than for symptomatic HTLV-III/LAV-infected children.

Because most HTLV-III/LAV-infected children become infected perinatally, it is to be expected that their mothers are infected with HTLV-III/LAV. Other family members may also be infected with HTLV-III/LAV and may have abnormal immunologic function.<sup>†</sup> Prospective evaluation of 16 asymptomatic HTLV-III/LAV-infected mothers of children diagnosed as having AIDS or ARC showed that 12 (75%) mothers developed AIDS or ARC during a 30-month follow-up period (6). Regardless of the immune status of the recipient, poliovaccine virus is often excreted by children vaccinated with oral poliovaccine (OPV) and may be transmitted to close contacts (19). Immune-deficient individuals (either recipients or contacts) have a higher risk of developing vaccine-associated poliomyelitis than normal individuals. There is no risk of transmitting the viruses contained in measles, mumps, rubella (MMR) vaccine to family members (20-22).

While the risks of vaccination are not known with certainty, potential risks may exist if HTLV-III/LAV-infected children are not vaccinated. If local outbreaks of measles occur in geographic areas in which there is both a cluster of unvaccinated children and a high prevalence of HTLV-III/LAV infection, the risk of measles for unvaccinated, HTLV-III/LAV-infected children may be high. Measles infection among patients with immune deficiency may be severe, protracted, and fatal (23).

<sup>†</sup>Such family members may have been infected by sexual contact with an HTLV-III/LAV-infected person, by parenteral exposure to infected blood (e.g., by sharing needles), or as hemophiliacs who received clotting factors, or by perinatal transmission.

## EXPERIENCES WITH IMMUNIZATION OF HTLV-III/LAV-INFECTED PERSONS

Some children infected perinatally with HTLV-III/LAV have received routine immunization with OPV and MMR before their illnesses were recognized. Out-patient medical records from New York City and Miami for 213 children with symptomatic HTLV-III/LAV infection (AIDS and ARC), presumably acquired during the perinatal period, were reviewed to determine immunization history and possible vaccine-associated adverse events (24,25). One hundred seventy-one children (80%) had received at least one dose of OPV and diphtheria and tetanus toxoids and pertussis vaccine (DTP). 95 (45%) had completed primary immunization with OPV and DTP (three doses and four doses, respectively), and 63 (30%) had received MMR or measles vaccine. Thirty-eight (39%) of 98 children who had available records of dates of immunization and onset of symptoms consistent with HTLV-III/LAV infection had received at least one live-virus vaccine after symptom onset. No serious or unusual adverse events were noted in the medical records of these children following immunization.

Only one adverse event following immunization of an HTLV-III/LAV-infected person has been documented. A 19-year-old asymptomatic army recruit received multiple immunizations during basic training, including primary immunization with small-pox vaccine (26). Two and one-half weeks later, he developed cryptococcal meningitis and was diagnosed as having AIDS. One and one-half weeks later, while being treated for meningitis, he developed lesions of disseminated vaccinia. He was treated with vaccinia immune globulin and recovered from vaccinia, but has since died of AIDS.

CDC has not received any reports of vaccine-associated poliomyelitis among HTLV-III/LAV-infected vaccine recipients or their contacts or among other persons known to be infected with HTLV-III/LAV. There have been no reports of serious adverse events following MMR administration from areas in which pediatric AIDS cases are occurring.

### IMMUNIZING CHILDREN WHO MAY BE INFECTED WITH HTLV-III/LAV: SPECIAL CONSIDERATIONS

Children born to women who are at risk of HTLV-III/LAV infection or who are known to be infected with HTLV-III/LAV should be evaluated for infection with the virus—including being tested for antibody (4,27). For asymptomatic children presenting for immunization, this evaluation and testing is not necessary to make decisions about immunizations. Children infected with HTLV-III/LAV are best cared for by pediatricians knowledgeable in the management of patients with this infection. Since little information is currently available on the safety and efficacy of immunizing children who may be infected with HTLV-III/LAV, special studies of these children need to be conducted.

## RECOMMENDATIONS

### Children with symptomatic HTLV-III/LAV infection

- A. Live-virus and live-bacterial vaccines (e.g., MMR, OPV, BCG) should not be given to children and young adults who are immunosuppressed in association with AIDS or other clinical manifestations of HTLV-III/LAV infection. For routine immunizations, these persons should receive inactivated poliovaccine (IPV) and should be excused for medical reasons from regulations requiring measles, rubella, and/or mumps immunization.
- B. Concerns have been raised that stimulation of the immune system by immunization with inactivated vaccines in these individuals might cause deterioration in immunologic function. However, such effects have not been noted thus far among children with AIDS or among other immunosuppressed individuals after immunization with inactivated vaccines. The potential benefits of immunization of these children outweigh the concerns of theoretical adverse events. Immunization with DTP, IPV, and *Haemophilus influenzae* type b vaccines is recommended in accordance with the ACIP recommendations, although immunization may be less effective than it would be for immunocompetent children (28-30).
- C. As with other conditions that produce chronic immunosuppression, the Committee recommends annual immunization with inactivated influenza vaccine for children over 6 months of age and one-time administration of pneumococcal vaccine for children over 2 years of age (31-33).
- D. Children and young adults with AIDS or other clinical manifestations of HTLV-III/LAV infection—as other immunosuppressed patients—may be at increased risk of having serious complications of infectious diseases, such as measles and varicella. Following significant exposure to measles or varicella, these persons should receive passive immunization with immune globulin (IG) or varicella-zoster immune globulin (VZIG), respectively (20,34).<sup>1</sup>

Children with previously diagnosed asymptomatic HTLV-III/LAV infection

- A. A small number of children and young adults known to be infected with HTLV-III/LAV but without overt clinical manifestations of immunosuppression have received live-virus vaccines without adverse consequences. Further experience needs to be monitored, but on the basis of data now available, the Committee believes that such persons should be vaccinated with MMR in accordance with ACIP recommendations (20-22). Vaccinees should be followed for possible adverse reactions and for the occurrence of vaccine-preventable diseases since immunization may be less effective than for uninfected persons.
- B. Available data suggest that OPV can be administered without adverse consequences to HTLV-III/LAV-infected children who do not have overt clinical manifestations of immunosuppression. However, because family members of such children may be immunocompromised due to AIDS or HTLV-III/LAV infection and therefore at increased risk of paralysis from contact with spread vaccine virus, it may be prudent to use IPV routinely to immunize asymptomatic children with previously diagnosed HTLV-III/LAV infection (28).
- C. Immunization with DTP and *Haemophilus influenzae* type b vaccines is recommended in accordance with ACIP recommendations (29,30).

<sup>1</sup>Some physicians administer full replacement doses of intravenous IG on a 2-4 week schedule to children with AIDS and other clinical manifestations of HTLV-III/LAV infection. This therapy may provide some protection against such diseases as measles and varicella.

#### Children not known to be infected with HTLV-III/LAV

Children and young adults not known to be infected with HTLV-III/LAV should be immunized in accordance with ACIP recommendations.

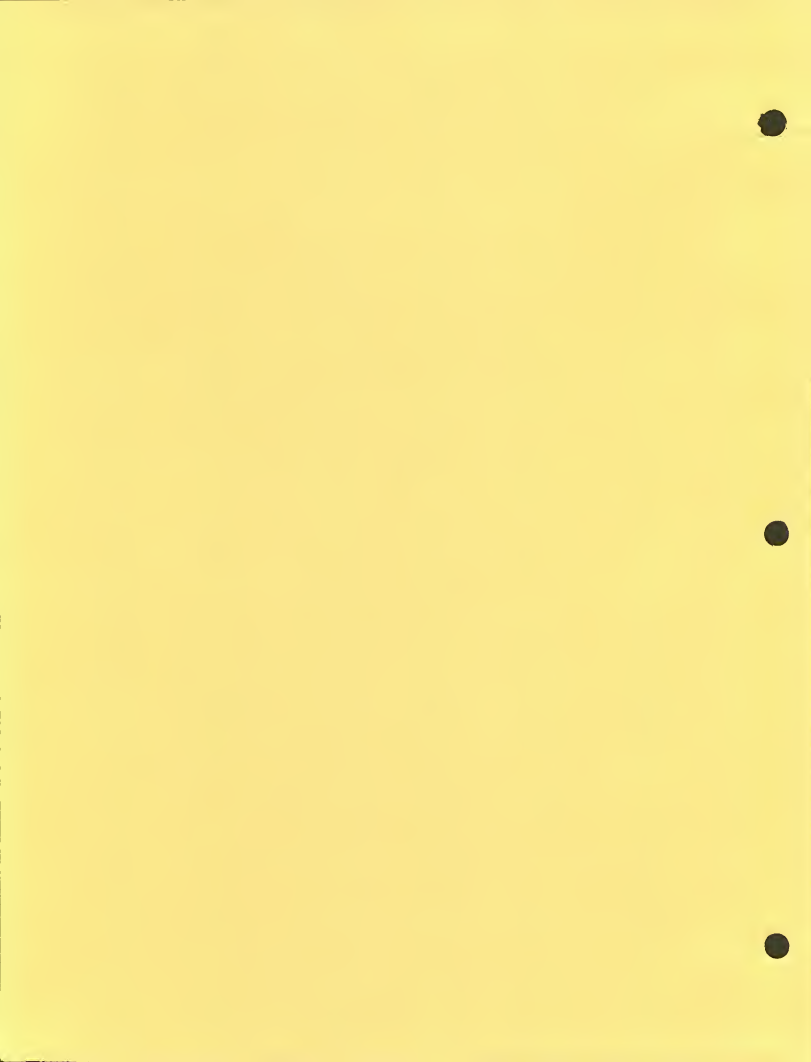
#### Children residing in the household of a patient with AIDS

Children whose household members are known to be immunocompromised due to AIDS or other HTLV-III/LAV infections should not receive OPV because vaccine viruses are excreted by the recipient of the vaccine and may be communicable to their immunosuppressed contacts. These children should receive IPV for routine immunization (28). Because extensive experience has shown that live, attenuated MMR vaccine viruses are not transmitted from vaccinated individuals to others, MMR may be given to a child residing in the household of a patient with AIDS (20-22).

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Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Immunization of Children Infected With  
Human Immunodeficiency Virus — Supplementary ACIP Statement**

The Immunization Practices Advisory Committee (ACIP) recently reviewed data both on the risks and benefits of immunizing children infected with human immunodeficiency virus (HIV) (1) and on severe and fatal measles in HIV-infected children in the United States (2). Since this review, the committee has revised its previous recommendations for measles vaccination and for mumps and rubella vaccination.

Previously published ACIP statements on immunizing HIV-infected children have recommended vaccinating children with asymptomatic HIV infection, but not those with symptomatic HIV infection (3). After considering reports of severe measles in symptomatic HIV-infected children, and in the absence of reports of serious or unusual adverse effects of measles, mumps, and rubella (MMR) vaccination in limited studies of symptomatic patients (4,5), the committee feels that administration of MMR vaccine should be considered for all HIV-infected children, regardless of symptoms. This approach is consistent with the World Health Organization's recommendation for measles vaccination (6).

If the decision to vaccinate is made, symptomatic HIV-infected children should receive MMR vaccine at 15 months, the age currently recommended for vaccination of children without HIV infection and for those with asymptomatic HIV infection. When there is an increased risk of exposure to measles, such as during an outbreak, these children should receive vaccine at younger ages. At such times, infants 6 to 11 months of age should receive monovalent measles vaccine and should be revaccinated with MMR at 12 months of age or older. Children 12-14 months of age should receive MMR and do not need revaccination (7).

The use of high-dose intravenous immune globulin (IGIV) (approximately 5 gm% protein) administered at regular intervals is being studied to determine whether it will prevent a variety of infections in HIV-infected children. It should be recognized that MMR vaccine may be ineffective if administered to a child who has received IGIV during the preceding 3 months.

Immune globulin (IG) (16.5 gm% protein) can be used to prevent or modify measles infection in HIV-infected persons if administered within 6 days of exposure. IG is especially indicated for measles-susceptible\* household contacts with asymptomatic HIV infection, particularly for those under 1 year of age, and for measles-susceptible pregnant women. The recommended dose is 0.25 mL/kg intramuscularly (maximum dose, 15 mL) (7).

In contrast, exposed symptomatic HIV-infected patients should receive IG prophylaxis regardless of vaccination status. The standard postexposure measles prophylaxis regimen for such patients is 0.5 mL/kg of IG intramuscularly (maximum dose, 15 mL) (7). This regimen corresponds to a dose of protein of approximately 82.5 mg/kg (maximum dose, 2,475 mg). Intramuscular IG may not be necessary if a patient with HIV infection is receiving 100-400 mg/kg IGIV at regular intervals and received the last dose within 3 weeks of exposure to measles. Based on the amount of protein that can be administered, high-dose IGIV may be as effective as IG given intramuscularly. However, no data exist on the efficacy of IGIV administered postexposure in preventing measles.

Although postexposure administration of globulins to symptomatic HIV-infected patients is recommended regardless of measles vaccine status, vaccination prior to exposure is desirable. Measles exposures are often unrecognized, and postexposure prophylaxis is not always possible.

\*Persons who are unvaccinated or do not have laboratory evidence or physician documentation of previous measles disease (7).

While recommendations for MMR vaccine have changed, those for other vaccines have not (3). A summary of the current ACIP recommendations for HIV-infected persons follows (Table 1). These recommendations apply to adolescents and adults with HIV infection as well as to HIV-infected children.

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7. Immunization Practices Advisory Committee. Measles prevention. *MMWR* 1987;36:409-18,423-5.

**TABLE 1. Recommendations for routine immunization of HIV-infected children — United States, 1988\***

| Vaccine            | HIV Infection      |                   |
|--------------------|--------------------|-------------------|
|                    | Known Asymptomatic | Symptomatic       |
| DTP <sup>†</sup>   | yes                | yes               |
| OPV <sup>‡</sup>   | no                 | no                |
| IPV <sup>§</sup>   | yes                | yes               |
| MMR <sup>**</sup>  | yes                | yes <sup>††</sup> |
| HbCV <sup>§§</sup> | yes                | yes               |
| Pneumococcal       | no                 | yes               |
| Influenza          | no                 | yes               |

\*See accompanying text and previous ACIP statement (3) for details.

<sup>†</sup>DTP = Diphtheria and tetanus toxoids and pertussis vaccine.

<sup>‡</sup>OPV = Oral, attenuated poliovirus vaccine; contains poliovirus types 1, 2, and 3.

<sup>§</sup>IPV = Inactivated poliovirus vaccine; contains poliovirus types 1, 2, and 3.

<sup>\*\*</sup>MMR = Live measles, mumps, and rubella viruses in a combined vaccine.

<sup>††</sup>Should be considered.

<sup>§§</sup>HbCV = *Haemophilus influenzae* type b conjugate vaccine.



## Diphtheria, Tetanus and Pertussis

### VACCINE AVAILABILITY

Two preparations are available from the Montana Immunization Program for public health use:

- Diphtheria and Tetanus Toxoids and Pertussis Vaccine (DTP)
- Tetanus and Diphtheria Toxoids, Adult Type (Td)

Both preparations contain comparable amounts of tetanus toxoid, but the diphtheria component in the adult type (Td) is only about 10-25% of that in standard DTP. Pediatric DT is available commercially, but is not provided by the Immunization Program.

#### Hints on DTP vaccine that may have exceeded storage temperatures:

DTP vaccine cannot be frozen. DTP vaccine that has been frozen may have solid particles in the solution which will not go into solution even with VIGOROUS shaking. DTP vaccine does routinely have a film which will settle to the bottom of the vial. Vigorous shaking will allow this material to return to suspension. All DTP vials should be shaken vigorously prior to use.

See the attached ACIP statement and Important Information Form. Also refer to the Adult Immunization Recommendation on Tetanus and diphtheria and the Control of Communicable Diseases in Man.



Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**Diphtheria, Tetanus, and Pertussis:  
Guidelines for Vaccine Prophylaxis and Other Preventive Measures**

*This revision of the Immunization Practices Advisory Committee (ACIP) statement on diphtheria, tetanus, and pertussis updates the statement issued in 1981 (1) and incorporates the 1984 supplementary statement on the risks of pertussis disease and pertussis vaccine for infants and children with personal histories of convulsions (2). It includes a review of the epidemiology of the three diseases, a description of the available immunobiologic preparations, and the appropriate immunization schedules. Also included are revisions in the schedule for combined diphtheria and tetanus toxoids (DT), when pertussis vaccine is contraindicated, and revisions in the recommendations on precautions and contraindications to vaccine use, on immunization for infants and children who have underlying neurologic disorders, and on tetanus prophylaxis in wound management.*

**INTRODUCTION**

Simultaneous immunization against diphtheria, tetanus, and pertussis during infancy and childhood has been a routine practice in the United States since the late 1940s. This practice has played a major role in markedly reducing the incidence rates of cases and deaths from each of these diseases.

**DIPHTHERIA**

At one time, diphtheria was common in the United States. More than 200,000 cases, primarily among children, were reported in 1921. Approximately 5%-10% of cases were fatal; the highest case-fatality ratios were in the very young and the elderly. Reported cases of diphtheria of all types declined from 306 in 1975 to 59 in 1979; most were cutaneous diphtheria reported from a single state. After 1979, cutaneous diphtheria was no longer reportable. From 1980 through 1983, only 15 cases of respiratory diphtheria were reported; 11 occurred among persons 20 years of age or older.

The current rarity of diphtheria in the United States is due primarily to the high level of appropriate immunization among children (96% of children entering school have received three or more doses of diphtheria and tetanus toxoids and pertussis vaccine [DTP]) and to an apparent reduction of the circulation of toxigenic strains of *Corynebacterium diphtheriae*. Most cases occur among unimmunized or inadequately immunized persons. The age distribution of recent cases and the results of serosurveys indicate that many adults in the United States are not protected against diphtheria. Thus, it appears that more emphasis should be placed on adult immunization programs.

Both toxigenic and nontoxigenic strains of *C. diphtheriae* can cause disease, but only strains that produce toxin cause myocarditis and neuritis. Furthermore, toxigenic strains are more often associated with severe or fatal illness in noncutaneous (respiratory or other mucosal surface) infections and are more commonly recovered from respiratory than from cutaneous infections.

*C. diphtheriae* can contaminate the skin of certain individuals, usually at the site of a wound. Although a sharply demarcated lesion with a pseudomembranous base often results, the appearance may not be distinctive, and the infection can be confirmed only by culture. Usually, other bacterial species can also be isolated. Cutaneous diphtheria has most commonly affected indigent adults and certain groups of Native Americans.

Complete immunization significantly reduces the risk of developing diphtheria, and immunized persons who develop disease have milder illnesses. Protection is thought to last at least 10 years. Immunization does not, however, eliminate carriage of *C. diphtheriae* in the pharynx or nose or on the skin.

**TETANUS**

The occurrence of tetanus in the United States has decreased markedly because of the routine use of tetanus toxin. Nevertheless, the number of reported cases has remained relatively constant in the last decade at an annual average of 90 cases. In 1983, 91 tetanus cases were reported from 29 states. In recent years, approximately two-thirds of patients have been 50 years of age or older. The age distribution of recent cases and the results of serosurveys indicate that many U.S. adults are not protected against tetanus. The disease has occurred almost exclusively among persons who are unimmunized or inadequately immunized or whose immunization histories are unknown or uncertain.

In 6% of tetanus cases reported during 1982 and 1983, no wound or other condition could be implicated. Nonacute skin lesions, such as ulcers, or medical conditions, such as abscesses, were reported in 17% of cases.

Neonatal tetanus occurs among infants born under unhygienic conditions to inadequately immunized mothers. Immune pregnant women confer protection to their infants through transplacental maternal antibody. From 1974 through 1983, 20 cases of neonatal tetanus were reported in the United States.

Spores of *Clostridium tetani* are ubiquitous. Serologic tests indicate that naturally acquired immunity to tetanus toxin does not occur in the United States. Thus, universal primary immunization, with subsequent maintenance of adequate antitoxin levels by means of appropriately timed boosters, is necessary to protect persons in all age groups. Tetanus toxoid is a highly effective antigen, and a completed primary series generally induces protective levels of serum antitoxin that persist for 10 or more years.

#### **PERTUSSIS**

General use of standardized pertussis vaccine has resulted in a substantial reduction in cases and deaths from pertussis disease. However, the annual number of reported cases has changed relatively little during the last 10 years, when annual averages of 1,835 cases and 10 fatalities have occurred. In 1983, 2,463 cases were reported; in 1981, the latest year for which final national mortality statistics are available from the National Center for Health Statistics, six deaths were recorded. More precise data do not exist, since many cases go unrecognized or unreported, and diagnostic tests for *Bordetella pertussis*—culture and direct-immunofluorescence assay (DFA)—may be unavailable, difficult to perform, or incorrectly interpreted.

For 1982 and 1983, 53% of reported illnesses from *B. pertussis* occurred among children under 1 year of age, and 78% among children under 5 years of age; 13 of 15 deaths reported to CDC occurred among children under 1 year old. Before widespread use of DTP, about 20% of cases and 50% of pertussis-related deaths occurred among children under 1 year old.

Pertussis is highly communicable (attack rates of over 90% have been reported in unimmunized household contacts) and can cause severe disease, particularly in very young children. Of patients under 1 year of age reported to CDC during 1982 and 1983, 75% were hospitalized; approximately 22% had pneumonia; 2% had one or more seizures; and 0.7% died. Because of the substantial risks of complications of the disease, completion of a primary series of DTP early in life is essential.

In older children and adults—including, in some instances, those previously immunized—infection may result in nonspecific symptoms of bronchitis or an upper respiratory tract infection, and pertussis may not be diagnosed because classic signs, especially the inspiratory whoop, may be absent. Older preschool-aged children and school-aged siblings who are not fully immunized and develop pertussis can be important sources of infection for young infants, the group at highest risk of disease and disease severity. The importance of the infected adult in overall transmission remains to be defined.

Controversy regarding use of pertussis vaccine led to a formal reevaluation of the benefits and risks of this vaccine. The analysis indicated that the benefits of the vaccine continue to outweigh its risks (3).

Because the incidence rate and severity of pertussis decrease with age, and because the vaccine may cause side effects and adverse reactions, pertussis immunization is not recommended for children after the seventh birthday, except under unusual circumstances (see **VACCINE USAGE**).

#### **PREPARATIONS USED FOR IMMUNIZATION**

Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins and are standardized for potency according to the regulations of the U.S. Food and Drug Administration (FDA). The LF content of each toxoid (quantity of toxoid as assessed by flocculation) may vary among different products. Because adverse reactions to diphtheria toxoid are apparently directly related to the quantity of antigen and to the age of the recipient, the concentration of diphtheria toxoid in preparations intended for use in adults is reduced.

Pertussis vaccine is a suspension of inactivated *B. pertussis* cells. Potency is assayed by comparison with the U.S. Standard Pertussis Vaccine in the intracerebral mouse protection test. The protective efficacy of pertussis vaccines in humans has been shown to correlate with the potency of vaccines.

Diphtheria and tetanus toxoids and pertussis vaccine, as single antigens or various combinations, are available as aluminum salt adsorbed preparations. Only tetanus toxoid is available in nonadsorbed (fluid) form. Although the rate of seroconversion is essentially equivalent with either type of tetanus toxoid, the adsorbed toxoid induces a more persistent antitoxin titer.

The two toxoids and the pertussis vaccine are currently available in the United States as the following preparations:

1. Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DTP) and Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use) (DT)<sup>\*</sup> are combinations for use in infants and children under 7 years old.

<sup>\*</sup>Distributed by Sclavo, Inc.

2. Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) (Td) is a combined preparation for use in persons 7 years old and older.
3. Pertussis Vaccine Adsorbed (P)<sup>†</sup>, Tetanus Toxoid (Fluid), Tetanus Toxoid Adsorbed (T), and Diphtheria Toxoid Adsorbed (D), are single-antigen products for use in instances when combined antigen preparations are not indicated.

Work is in progress to develop an effective acellular pertussis vaccine with a reduced reaction rate. Current research is directed toward development of a vaccine consisting principally of one or more of the bacterial components thought to provide protection. Prominent candidate antigens include filamentous hemagglutinin and lymphocytosis promoting factor (pertussis toxin). However, several years will be necessary to complete development and to document the potency, safety, and efficacy of a new vaccine.

#### VACCINE USAGE

The standard single-dose volume of DTP, DT, Td, single-antigen adsorbed preparations of pertussis vaccine, tetanus toxoid, and diphtheria toxoid, and the nonadsorbed tetanus toxoid is 0.5 ml. Adsorbed preparations should be administered intramuscularly (IM). Vaccine administration by jet injection may be associated with more frequent local reactions. (See also: ACIP: General recommendations on immunization. *MMWR* 1983;32:1-8,13-7.)

#### Primary Immunization

Children 6 weeks through 6 years old (up to the seventh birthday) (Table 1). One dose of DTP should be given IM on four occasions—the first three doses at 4- to 8-week intervals, beginning when the infant is approximately 6 weeks-2 months old. The fourth dose is given approximately 6-12 months after the third to maintain adequate immunity for the ensuing preschool years. This dose is an integral part of the primary immunizing course. If a contraindication to pertussis vaccination exists (see **PRECAUTIONS AND CONTRAINDICATIONS**), DT should be substituted for DTP as outlined under **Special Considerations** below.

Persons 7 years old and older (Table 2). Pertussis-containing preparations are not recommended routinely in these age groups. A series of three doses of Td should be given IM; the second dose is given 4-8 weeks after the first; and the third dose, 6-12 months after the second. Td rather than DT is the agent of choice for immunization of all patients 7 years old and older, because side effects from higher doses of diphtheria toxoid are more common in older children and adults.

**Interruption of primary immunization schedule.** Interrupting the recommended schedule or delaying subsequent doses probably does not lead to a reduction in the level of immunity reached on completion of the primary series. Therefore, there is no need to restart a series regardless of the time elapsed between doses.

**TABLE 1. Routine diphtheria, tetanus, and pertussis immunization schedule summary for children under 7 years old — United States, 1985\***

| Dose                | Age/Interval <sup>†</sup>   | Product           |
|---------------------|---|-------------------|
| Primary 1           | 6 weeks old or older  | DTP <sup>†¶</sup> |
| Primary 2           | 4-8 weeks after first dose <sup>§</sup>   | DTP <sup>¶</sup>  |
| Primary 3           | 4-8 weeks after second dose <sup>§</sup>  | DTP <sup>¶</sup>  |
| Primary 4           | 6-12 months after third dose <sup>§</sup>   | DTP <sup>¶</sup>  |
| Booster             | 4-6 years old, before entering kindergarten or elementary school (not necessary if fourth primary immunizing dose administered on or after fourth birthday) | DTP <sup>¶</sup>  |
| Additional boosters | Every 10 years after last dose  | Td                |

\*Important details are in the text.

<sup>†</sup>Customarily begun at 8 weeks of age, with second and third doses given at 8-week intervals.

<sup>§</sup>Prolonging the interval does not require restarting series.

<sup>¶</sup>DT, if pertussis vaccine is contraindicated. If the child is 1 year of age or older at the time the primary dose is given, a third dose 6-12 months after the second completes primary immunization with DT.

<sup>†</sup>Distributed by the Biologics Products Program, Michigan Department of Public Health, for use within that state; may be available for use outside Michigan under special circumstances by consultation with that program.

**TABLE 2. Routine diphtheria and tetanus immunization schedule summary for persons 7 years old and older — United States, 1985\***

| Dose       | Age/interval                               | Product |
|------------|--|---------|
| Primary 1  | First dose                                 | Td      |
| Primary 2  | 4-8 weeks after first dose <sup>†</sup>    | Td      |
| Primary 3  | 6-12 months after second dose <sup>†</sup> | Td      |
| Boosters * | Every 10 years after last dose             | Td      |

\*Important details are in the text.

<sup>†</sup>Prolonging the interval does not require restarting series.

#### Booster Immunization

**Children 4-6 years old (up to the seventh birthday).** Those who received all four primary immunizing doses before the fourth birthday should receive a single dose of DTP just before entering kindergarten or elementary school. This booster dose is not necessary if the fourth dose in the primary series was given on or after the fourth birthday.

**Persons 7 years old and older.** Tetanus toxoid should be given with diphtheria toxoid as Td every 10 years. If a dose is given sooner as part of wound management, the next booster is not needed for 10 years thereafter (see **TETANUS PROPHYLAXIS IN WOUND MANAGEMENT**). More frequent boosters are not indicated and have been reported to result in an increased occurrence and severity of adverse reactions. One means of ensuring that persons receive boosters every 10 years is to vaccinate persons routinely at mid-decade ages, i.e., 15 years, 25 years, 35 years, etc.

#### Special Considerations

**Children with a contraindication to pertussis vaccination (see PRECAUTIONS AND CONTRAINDICATIONS).** For children under 7 years old with a contraindication to pertussis vaccine, DT should be used rather than DTP. To ensure that there will be no interference with the antigens from maternal antibodies, unimmunized children under 1 year of age receiving their first DT dose should receive a total of four doses of DT as the primary series, the first three doses at 4- to 8-week intervals and the fourth dose 6-12 months later (similar to the recommended DTP schedule). If further doses of pertussis vaccine become contraindicated after beginning a DTP series in the first year of life, DT should be substituted for each of the remaining scheduled DTP doses.

Unimmunized children 1 year of age or older for whom DTP is contraindicated should receive two doses of DT 4-8 weeks apart, followed by a third dose 6-12 months later to complete the primary series. Children 1 year of age or older who have received one or two doses of DT or DTP and for whom further pertussis vaccine is contraindicated should receive a total of three doses of a preparation containing diphtheria and tetanus toxoids, with the third dose administered 6-12 months after the second dose.

Children who complete a primary series of DT before the fourth birthday should receive a single dose of DT just before entering kindergarten or elementary school. This dose is not necessary if the last dose of the primary series was given on or after the fourth birthday.

**Pertussis immunization for persons 7 years old or older.** Routine immunization against pertussis is not recommended for persons 7 years old and older. In exceptional cases, such as persons with chronic pulmonary disease exposed to children with pertussis or health-care personnel exposed during nosocomial or community outbreaks, a booster dose of adsorbed pertussis vaccine may be considered. A reduced dose is used for adults (4). Routine pertussis vaccination of hospital personnel is not recommended.

**Persons recovering from tetanus or diphtheria.** Tetanus or diphtheria infection may not confer immunity; therefore, active immunization should be initiated at the time of recovery from the illness, and arrangements made to ensure that the remaining doses of a primary series are administered as early as possible.

**Children recovering from pertussis.** Children who have recovered from culture-confirmed pertussis need not receive further doses of pertussis vaccine. Lacking culture confirmation of the diagnosis, DTP immunization should be completed, because a pertussis-like syndrome may have been caused by other *Bordetella* species, chlamydia, or some viruses.

**Neonatal tetanus prevention.** There is no evidence that tetanus and diphtheria toxoids are teratogenic. A previously unimmunized pregnant woman who may deliver her child under unhygienic circumstances or surroundings should receive two properly spaced doses of Td before delivery, preferably during the last two trimesters. Incompletely immunized pregnant women should complete the three-dose series. Those immunized more than 10 years previously should have a booster dose.

**Adult immunization with Td** Limited serosurveys done since 1977 indicate that the proportion of the population lacking protective levels of circulating antitoxin against diphtheria and tetanus increases with increasing age and that at least 40% of persons 60 years of age or older lack protective levels of antitoxins. Every visit of an adult to a health-care provider should be an opportunity to assess the patient's immunization status and, if indicated, to provide protection against tetanus and diphtheria using the combined toxoid, Td. Adults with uncertain histories of a complete primary series should receive a primary series. To ensure continued adequate protection in the individual, booster doses of Td could be given routinely at mid-decade ages, i.e., 15 years, 25 years, 35 years, etc.

#### **Use of Single-Antigen Preparations**

Multiple-antigen preparations should be used, unless there is a contraindication to one or more antigens in a preparation.

A single-antigen adsorbed pertussis vaccine preparation may be used to complete immunization against pertussis for children under 7 years of age who have received fewer than the recommended number of doses of pertussis vaccine but have received the recommended number of doses of diphtheria and tetanus toxoids for their age. Alternatively, doses of DTP can be given for protection against pertussis, although it is suggested that the total number of doses of diphtheria and tetanus toxoids not exceed six each before the seventh birthday.

Available data do not indicate substantially more reactions following receipt of Td than following receipt of single-antigen, adsorbed tetanus toxoid. Furthermore, adults, in general, are even less likely to have adequate circulating levels of diphtheria antitoxin than adequate circulating levels of tetanus antitoxin. The routine use of Td in all medical settings, e.g., private practice, clinics, and emergency rooms, for all persons 7 years of age or older requiring primary immunization or booster doses will improve levels of protection against both tetanus and diphtheria, especially among adults.

#### **SIDE EFFECTS AND ADVERSE REACTIONS**

Local reactions, generally erythema and induration with or without tenderness, are common after the administration of vaccines containing diphtheria, tetanus, or pertussis antigens. Occasionally, a nodule may be palpable at the injection site of adsorbed products for several weeks. Abscesses at the site of injection have been reported (6-10 per million doses). Mild systemic reactions, such as fever, drowsiness, fretfulness, and anorexia, occur quite frequently. These reactions are significantly more common following DTP than following DT, are usually self-limited, and need no therapy other than, perhaps, symptomatic treatment (e.g., antipyretics).

Moderate to severe systemic events, such as fever of 40.5 C (105 F) or higher, persistent, inconsolable crying lasting 3 hours or more, unusual high-pitched crying, collapse, or convulsions, occur relatively infrequently. Other more severe neurologic complications, such as a prolonged convulsion or an encephalopathy, occasionally fatal, have been reported to be associated with DTP administration, although rarely.

Approximate rates for adverse events following receipt of DTP vaccine (regardless of dose number in the series) are indicated in Table 3 (5,6).

The frequency of local reactions and fever following DTP vaccination is significantly higher with increasing numbers of doses of DTP, while other mild to moderate systemic reactions (e.g., fretfulness, vomiting) are significantly less frequent (5). If local redness of 2.5 cm or greater occurs, the likelihood of recurrence after another DTP dose increases significantly (7).

In the National Childhood Encephalopathy Study (NCES), a large, case-control study in England (6), children 2-35 months of age with serious, acute neurologic disorders, such as encephalopathy or complicated convulsion(s), were more likely to have received DTP in the 7 days preceding onset than their age-, sex-, and neighborhood-matched controls. Among children known to be neurologically normal before entering the study, the relative risk<sup>§</sup> of a neurologic illness occurring within the 7-day period following receipt of DTP dose, compared to children not receiving DTP vaccine in the 7-day period before onset of their illness, was 3.3 ( $p < 0.001$ ). Within this 7-day period, the risk was significantly increased for immunized children only within 3 days of vaccination (relative risk 4.2,  $p < 0.001$ ). The relative risk for illness occurring 4-7 days after vaccination was 2.1 ( $0.05 < p < 0.1$ ). The attributable risk estimates for a serious acute neurologic disorder within 7 days after DTP vaccine (regardless of outcome) was one in 110,000 doses of DTP, and for a permanent neurologic deficit, one in 310,000 doses. No specific clinical syndrome was identified. Overall, DTP vaccine accounted for only a small proportion of cases of serious neurologic disorders reported in the population studied.

Although there are uncertainties in the reported studies, recent data suggest that infants and young children who have had previous convulsions (whether febrile or nonfebrile) are more likely to have seizures following DTP than those without such histories (8).

<sup>§</sup>Relative risk was estimated by odds ratio.

**TABLE 3. Adverse events occurring within 48 hours of DTP immunizations**

| Event   | Frequency*      |
|---|-----------------|
| <b>Local</b>  |                 |
| Redness   | 1/3 doses       |
| Swelling  | 2/5 doses       |
| Pain  | 1/2 doses       |
| <b>Mild/moderate systemic</b>                               |                 |
| Fever $\geq 38$ C (100.4 F)                                 | 1/2 doses       |
| Drowsiness  | 1/3 doses       |
| Fretfulness   | 1/2 doses       |
| Vomiting  | 1/15 doses      |
| Anorexia  | 1/5 doses       |
| <b>More serious systemic</b>                                |                 |
| Persistent, inconsolable crying<br>duration $\geq 3$ hours) | 1/100 doses     |
| High-pitched, unusual cry                                   | 1/900 doses     |
| Fever $\geq 40.5$ C ( $\geq 105$ F)                         | 1/330 doses     |
| Collapse (hypotonic-<br>hyporesponsive episode)             | 1/1,750 doses   |
| Convulsions<br>(with or without fever)                      | 1/1,750 doses   |
| Acute encephalopathy†                                       | 1/110,000 doses |
| Permanent neurologic deficit†                               | 1/310,000 doses |

\*Number of adverse events per total number of doses regardless of dose number in DTP series.

†Occurring within 7 days of DTP immunization.

Rarely, an anaphylactic reaction (i.e., hives, swelling of the mouth, difficulty breathing, hypotension, or shock) has been reported after receiving preparations containing diphtheria, tetanus, and/or pertussis antigens. The ACIP finds no good evidence for a causal relationship between DTP and hemolytic anemia or thrombocytopenic purpura.

Arthus-type hypersensitivity reactions, characterized by severe local reactions (generally starting 2-8 hours after an injection), may follow receipt of tetanus toxoid, particularly in adults who have received frequent (e.g., annual) boosters of tetanus toxoid. A few cases of peripheral neuropathy have been reported following tetanus toxoid administration, although a causal relationship has not been established.

Sudden infant death syndrome (SIDS) has occurred in infants following administration of DTP. A large case-control study of SIDS in the United States showed that receipt of DTP was not causally related to SIDS (9). It should be recognized that the first three primary immunizing doses of DTP are usually administered to infants 2-6 months old and that approximately 85% of SIDS cases occur at ages 1-6 months, with the peak incidence occurring at 6 weeks-4 months of age. By chance alone, some SIDS victims can be expected to have recently received vaccine.

Onset of infantile spasms has occurred in infants who have recently received DTP or DT. Analysis of data from the NCES on children with infantile spasms showed that receipt of DTP or DT was not causally related to infantile spasms (10). The incidence of onset of infantile spasms increases at 3-9 months of age, the time period in which the second and third doses of DTP are generally given. Therefore, some cases of infantile spasms can be expected to be related by chance alone to recent receipt of DTP.

#### Reporting of Adverse Events

Reporting by parents and patients of all adverse events occurring within 4 weeks of antigen administration should be encouraged. Adverse events that require a visit to a health-care provider should be reported by health-care providers to manufacturers and local or state health departments. The information will be forwarded to an appropriate federal agency (the Bureau of Biologics Research and Review, FDA, or CDC).

#### COMMENTS ON USING REDUCED DOSAGE SCHEDULES OR MULTIPLE SMALL DOSES

The ACIP recommends giving only the full dose of DTP; if a specific contraindication to DTP exists, none should be given. In the United States, the full course of primary immunization is considered to be four 0.5-ml doses of DTP.



Concern about adverse events following pertussis vaccination has led some practitioners to reduce the volume of DTP administered to less than 0.5 ml per dose in an attempt to reduce side effects. There is no evidence that a reduction in dosage decreases the frequency of severe events, such as seizures, hypotonic-hyporesponsive episodes, and encephalopathy. The mechanisms for these reactions are not known. Some studies reported significantly lower rates of local reactions to one-half the recommended dose (0.25 ml), compared to those following a full dose (7,11). A recent study also showed significantly lower pertussis serologic responses after the second and third half-doses, although the differences were small (11). This investigation used pertussis agglutinins as a measure of clinical protection; however, agglutinins are not absolute measures of clinical protection against pertussis disease. Furthermore, there is no evidence that the low screening titer used in this investigation (1:16) is indicative of protection. Currently, there are no reliable measures of efficacy other than clinical protection. Further evidence against the use of reduced doses comes from earlier studies of vaccine (12,13) with potency equivalent to that of half-doses of current vaccine. Attack rates of pertussis for exposed household contacts who received a lower potency vaccine (equivalent to a half-dose of the current vaccine) were approximately twice as high as attack rates for exposed household contacts who had received vaccines of potency equivalent to full doses of current vaccine (29%, compared to 14% or lower).

The use of an increased number of reduced-volume doses of DTP to equal the total volume of the five recommended doses of DTP vaccine is not recommended. It is unknown whether such a practice reduces the likelihood of vaccine-related events. In addition, by increasing the number of immunizations, the likelihood of a temporally associated but etiologically unrelated event may be enhanced.

Neither the use of reduced individual DTP doses nor the use of multiple doses of reduced volume that, in total, equal a full immunizing dose has been adequately studied. Neither the efficacy of such practices in reducing the frequency of associated serious adverse events nor the resulting protection against disease have been determined.

#### **SIMULTANEOUS ADMINISTRATION OF VACCINES**

The simultaneous administration of DTP, oral polio virus vaccine (OPV), and/or measles-mumps-rubella vaccine (MMR) has resulted in seroconversion rates and rates of side effects similar to those observed when the vaccines are administered separately (14). Therefore, if there is any doubt that a vaccine recipient will return for further vaccine doses, the ACIP recommends the simultaneous administration of all vaccines appropriate to the age and previous vaccination status of the recipient. This would especially include the simultaneous administration of DTP, OPV, and MMR to such persons at 15 months of age or older.

#### **PRECAUTIONS AND CONTRAINDICATIONS**

A febrile illness is reason to defer routine vaccination. Minor illness, such as mild upper respiratory infection, should not ordinarily be a reason for postponing vaccination. A history of prematurity generally is not a reason to defer vaccination (15).

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines. Short-term (less than 2 weeks) corticosteroid therapy or intra-articular, bursal, or tendon injections with corticosteroids should not be immunosuppressive. Although no specific studies with pertussis vaccine are available, if immunosuppressive therapy will be discontinued shortly, it would be reasonable to defer immunization until the patient has been off therapy for 1 month (16); otherwise, the patient should be vaccinated while still on therapy.

When an infant or child returns for the next dose of DTP, the parent should be questioned about any adverse events occurring after the previous dose.

#### **Pertussis-Containing Preparations**

**Absolute contraindications.** If any of the following adverse events occur after DTP or single-antigen pertussis vaccination, further vaccination with a vaccine containing pertussis antigen is contraindicated:

1. Allergic hypersensitivity
2. Fever of 40.5 C (105 F) or greater within 48 hours.
3. Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours.
4. Persisting, inconsolable crying lasting 3 hours or more or an unusual, high-pitched cry occurring within 48 hours.
5. Convulsion(s) with or without fever occurring within 3 days. (All children with convulsions, especially those with convulsions occurring within 4-7 days of receipt of DTP, should be fully evaluated to clarify their medical and neurologic status before a decision is made on initiating or continuing vaccination with DTP [see next section, item 3]).
6. Encephalopathy occurring within 7 days; this includes severe alterations in consciousness with generalized or focal neurologic signs. (A small but significantly increased risk of encephalopathy has been shown only

within the 3-day period following DTP receipt. However, most authorities believe that an encephalopathy occurring within 7 days of DTP should be considered a contraindication to further doses of DTP.)

**Immunization of infants and young children who have underlying neurologic disorders.** The presence of a neurologic condition characterized by changing developmental or neurologic findings, regardless of whether a definitive diagnosis has been made, is also considered a contraindication to receipt of pertussis vaccine, because administration of DTP may coincide with or possibly even aggravate manifestations of the disease. Such disorders include uncontrolled epilepsy, infantile spasms, and progressive encephalopathy. Stable conditions, such as cerebral palsy and developmental delay, are not considered contraindications to receipt of pertussis vaccination.

Although there are uncertainties in the reported studies, recent data suggest that infants and young children who have had previous convulsions (whether febrile or nonfebrile) are more likely to have seizures following DTP receipt than those without such histories (8). A convulsion within 3 days of DTP receipt in a child with a history of convulsion(s) may be initiated by fever caused by the vaccine in a child prone to febrile convulsions, induced by the pertussis component, or unrelated to the vaccination. Available data do not indicate that seizures alone, temporally associated with DTP administration, induce permanent brain damage in these children.

Whether to administer DTP to children with proven or suspected underlying neurologic disorders, and when, must be decided on an individual basis. An important consideration is the current low frequency of pertussis reported in most areas of the United States, indicating a relatively low risk of exposure. Other considerations include the current near absence of diphtheria in the United States and the low risk that an infant will acquire an infection with *C. tetani*. Based on these considerations and the nature of the child's disorder, the following approaches are recommended:

1. **Infants as yet unimmunized who are suspected of having underlying neurologic disease.** Possible latent central nervous system disorders that are suspected because of perinatal complications or other phenomena may become evident as they evolve over time. Because DTP administration may coincide with onset of overt manifestations of such disorders and result in confusion about causation, it is prudent to delay initiation of immunization with DTP or DT (but not OPV) until further observation and study have clarified the child's neurologic status. In addition, the effect of treatment, if any, can be assessed. The decision whether to commence immunization with DTP or DT should be made no later than the child's first birthday. In making this decision, it should be recognized that children with severe neurologic disorders may be at enhanced risk of exposure to pertussis from institutionalization or from attendance at clinics and special schools in which many of the children may be unimmunized. In addition, because of neurologic handicaps, these children may be in greater jeopardy from complications of the disease.
2. **Infants and children with neurologic events temporally associated with DTP.** Infants and children who experience a seizure within 3 days of receipt of DTP or an encephalopathy within 7 days should not receive further pertussis vaccine, even though cause and effect may not be established (see PRECAUTIONS AND CONTRAINDICATIONS).
3. **Incompletely immunized children with neurologic events occurring between doses.** Infants and children who have received one or more doses of DTP and who experience a neurologic disorder, e.g., a seizure, temporally unassociated with the administration of vaccine but before the next scheduled dose, present a special problem. If the seizure or other disorder occurs before the first birthday and completion of the first three doses of the primary series of DTP, deferral of further doses of DTP or DT (but not OPV) is recommended until the infant's status has been clarified. The decision whether to use DTP or DT to complete the series should be made no later than the child's first birthday and should take into consideration the nature of the child's problem and the benefits and risks of the vaccine. If the seizure or other disorder occurs after the first birthday, the child's neurologic status should be evaluated to ensure the disorder is stable before a subsequent dose of DTP is given (see next section).
4. **Infants and children with stable neurologic conditions.** Infants and children with stable neurologic conditions, including well-controlled seizures, may be vaccinated. The occurrence of single seizures (temporally unassociated with DTP) in infants and young children, while necessitating evaluation, need not contraindicate DTP immunization, particularly if the seizures can be satisfactorily explained. Anticonvulsant prophylaxis should be considered when giving DTP to such children. Parents of infants and children with histories of convulsions should be made aware of the slightly increased chance of postimmunization seizures.
5. **Children with resolved or corrected neurologic disorders.** DTP administration is recommended for infants with certain neurologic problems that have clearly subsided without residua or have been corrected, such as neonatal hypocalcemic tetany or hydrocephalus (following placement of a shunt and without seizures).

Immunization of infants and young children with family histories of convulsion or other central nervous system disorders. The ACIP, after evaluating the evidence available concerning the risk of a neurologic illness following pertussis vaccination of a child with a family history of convulsion or other central nervous system disorder, does not believe that such a history is a contraindication to pertussis vaccination.

#### Preparations Containing Diphtheria Toxoid and Tetanus Toxoid

The only contraindication to tetanus and diphtheria toxoids is a history of a neurologic or severe hypersensitivity reaction following a previous dose. Immunization with tetanus and diphtheria toxoids is not known to be associated with an increased risk of convulsions. Local side effects alone do not preclude continued use. If an anaphylactic reaction to a previous dose of tetanus toxoid is suspected, intradermal skin testing with appropriately diluted tetanus toxoid may be useful before a decision is made to discontinue tetanus toxoid immunization (17). In one study, 94 of 95 persons giving histories of anaphylactic symptoms following a previous tetanus toxoid dose were nonreactive following intradermal testing and tolerated a further tetanus toxoid challenge without a reaction (17). One person had immediate erythema and induration following skin testing but tolerated a full intramuscular dose without adverse effects. Mild, nonspecific skin-test reactivity to tetanus toxoid, particularly if used undiluted, appears to be fairly common. Most vaccinees develop inconsequential cutaneous delayed hypersensitivity to the toxoid.

Persons who experienced Arthus-type hypersensitivity reactions or fever greater than 39.4 C (103 F) following a prior dose of tetanus toxoid usually have very high serum tetanus antitoxin levels and should not be given even emergency doses of Td more frequently than every 10 years, even if they have a wound that is neither clean nor minor.

If a contraindication to using tetanus toxoid-containing preparations exists in a person who has not completed a primary immunizing course of tetanus toxoid and other than a clean, minor wound is sustained, *only* passive immunization should be given using tetanus immune globulin (TIG) (see **TETANUS PROPHYLAXIS IN WOUND MANAGEMENT**).

Although there is no evidence that tetanus and diphtheria toxoids are teratogenic, waiting until the second trimester of pregnancy to administer Td is a reasonable precaution to minimize any theoretical concern.

#### DIPHTHERIA PROPHYLAXIS FOR CASE CONTACTS

All close contacts, household and other, with less than three doses of diphtheria toxoid should receive an immediate dose of a diphtheria toxoid-containing preparation and should complete the series according to schedule (Tables 1 and 2). Close contacts with three or more doses who have not received a dose of a preparation containing diphtheria toxoid within the previous 5 years should receive a booster dose of a diphtheria toxoid-containing preparation appropriate for their age.

All close contacts should be examined daily for 7 days for evidence of disease. Asymptomatic unimmunized or inadequately immunized close contacts should receive prompt chemoprophylaxis with either an IM injection of benzathine penicillin (600,000 units for persons under 6 years old and 1,200,000 units for those 6 years old or older) or a 7- to 10-day course of oral erythromycin (children: 40 mg/kg/day; adults: 1 g/day). Erythromycin may be slightly more effective, but IM benzathine penicillin may be preferred, since it avoids possible problems of noncompliance with a multiday oral drug regimen. Bacteriologic cultures before and after antibiotic prophylaxis may be useful in the follow-up and management of contacts. Identified untreated carriers of toxigenic *C. diphtheriae* should receive antibiotics as recommended above for unimmunized household contacts. Those who continue to harbor the organism after either penicillin or erythromycin should receive an additional 10-day course of oral erythromycin.

Even when close surveillance of unimmunized close contacts is impossible, the use of equine diphtheria antitoxin is not generally recommended because of the risks of allergic reaction to horse serum. Immediate hypersensitivity reactions occur in about 7%, and serum sickness, in 5% of adults receiving the recommended prophylactic dose of equine antitoxin. The risk of adverse reactions to equine antitoxin must be weighed against the small risk of diphtheria occurring in an unimmunized household contact who receives chemoprophylaxis. If antitoxin is to be used, the usually recommended dose is 5,000-10,000 units IM—after appropriate testing for sensitivity—at a site different from that of toxoid injection. The immune response to simultaneous diphtheria antitoxin and toxoid inoculation is unlikely to be impaired, but this has not been adequately studied.

Cases of cutaneous diphtheria generally are caused by infections with nontoxigenic strains of *C. diphtheriae*. However, a lesion suspected of being cutaneous diphtheria should be considered to be caused by a toxigenic strain until proven otherwise. Recommendations for prophylaxis of close case contacts are the same as for respiratory diphtheria, since cutaneous diphtheria may be more contagious than respiratory infection for close contacts. If a cutaneous case is known to be due to a nontoxigenic strain, routine investigation or prophylaxis of contacts is not necessary.

## TETANUS PROPHYLAXIS IN WOUND MANAGEMENT

Chemoprophylaxis against tetanus is neither practical nor useful in managing wounds; wound cleaning, debridement when indicated, and proper immunization are important. The need for tetanus toxoid (active immunization), with or without tetanus immune globulin (TIG) (passive immunization), depends on both the condition of the wound and the patient's immunization history (Table 4; see also PRECAUTIONS AND CONTRAINDICATIONS). Rarely has tetanus occurred among persons with a documented primary series of toxoid injections.

A thorough attempt must be made to determine whether a patient has completed primary immunization. Patients with unknown or uncertain previous immunization histories should be considered to have had no previous tetanus toxoid doses. Persons who had military service since 1941 can be considered to have received at least one dose; although most may have completed a primary series of tetanus toxoid, this cannot be assumed for each individual. Patients who have not completed a primary series may require tetanus toxoid and passive immunization at the time of wound cleaning and debridement (Table 4).

**TABLE 4. Summary guide to tetanus prophylaxis in routine wound management — United States, 1985\***

| History of adsorbed tetanus toxoid (doses) | Clean, minor wounds |     | All other wounds <sup>†</sup> |     |
|--|---------------------|-----|-------------------------------|-----|
|  | Td <sup>§</sup>     | TIG | Td <sup>§</sup>               | TIG |
| Unknown or < three                         | Yes                 | No  | Yes                           | Yes |
| ≥ three <sup>¶</sup>                       | No**                | No  | No <sup>††</sup>              | No  |

\*Important details are in the text.

<sup>†</sup>Such as, but not limited to, wounds contaminated with dirt, feces, soil, saliva, etc.; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns and frostbite.

<sup>§</sup>For children under 7 years old; DTP (DT, if pertussis vaccine is contraindicated) is preferred to tetanus toxoid alone. For persons 7 years old and older, Td is preferred to tetanus toxoid alone.

<sup>¶</sup>If only three doses of fluid toxoid have been received, a fourth dose of toxoid, preferably an adsorbed toxoid, should be given.

\*\*Yes, if more than 10 years since last dose.

<sup>††</sup>Yes, if more than 5 years since last dose. (More frequent boosters are not needed and can accentuate side effects.)

Available evidence indicates that complete primary immunization with tetanus toxoid provides long-lasting protection—10 years or more in most recipients. Consequently, after complete primary tetanus immunization, boosters—even for wound management—need to be given only every 10 years when wounds are minor and uncontaminated. For other wounds, a booster is appropriate if the patient has not received tetanus toxoid within the preceding 5 years. Antitoxin antibodies develop rapidly in persons who have previously received at least two doses of tetanus toxoid.

Td is the preferred preparation for active tetanus immunization in wound management of patients 7 years old or older. This is to enhance diphtheria protection, since a large proportion of adults are susceptible. Thus, by taking advantage of acute health-care visits, such as for wound management, some patients can be protected who otherwise would remain susceptible. For routine wound management of children under 7 years old who are not adequately immunized, DTP should be used instead of single-antigen tetanus toxoid. If pertussis vaccine is contraindicated or individual circumstances are such that potential febrile reactions following DTP might confound the management of the patient, DT may be used. For inadequately immunized patients of all ages, completion of primary vaccination at the time of discharge or at follow-up visits should be ensured (Tables 1 and 2).

If passive immunization is needed, human TIG is the product of choice. It provides longer protection than antitoxin of animal origin and causes few adverse reactions. The currently recommended prophylactic dose of TIG for wounds of average severity is 250 units IM. When tetanus toxoid and TIG are given concurrently, separate syringes and separate sites should be used. The ACIP recommends the use of only adsorbed toxoid in this situation.

## PERTUSSIS PROPHYLAXIS FOR CASE CONTACTS

Spread of pertussis can be limited by decreasing infectivity of the patient and by protecting close contacts of that patient. To reduce infectivity as quickly as possible, a course of oral erythromycin (children: 40 mg/kg/day; adults: 1 g/day) or trimethoprim/sulfamethoxazole (children: trimethoprim 8 mg/kg/day, sulfamethoxazole 40 mg/kg/day; adults: trimethoprim 320 mg/day, sulfamethoxazole 1,600 mg/day) is recommended for patients with clinical pertussis. The antibiotic should be administered for 14 days to minimize any chance of antibiotic failure. Chemotherapy, however, probably does not affect the duration or severity of disease.

There are two approaches for protecting close contacts (such as children exposed in a household or day-care center) of patients with pertussis—active immunization and chemoprophylaxis. Close contacts under 7 years old who have not completed the four-dose primary series of DTP injections or who have not received a dose of DTP within 3 years of exposure should be given a dose of vaccine and should complete a primary series with the minimal intervals (Table 1). While the usefulness of chemoprophylaxis has not been well demonstrated, it may be prudent to consider a 14-day course of erythromycin or trimethoprim/sulfamethoxazole for close contacts under 1 year old, regardless of immunization status, and for unimmunized close contacts under 7 years old.

Prophylactic postexposure passive immunization is not recommended. Studies have shown that use of human pertussis immune globulin neither prevents illness nor reduces its severity. This product is no longer available in the United States.

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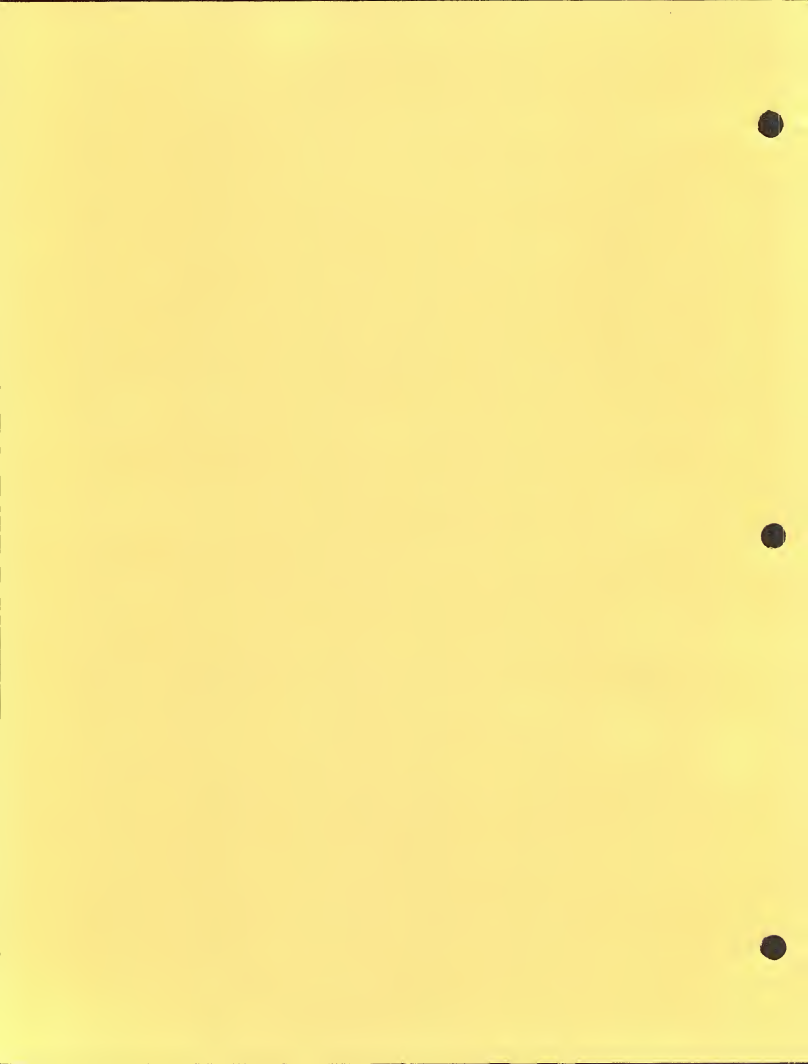
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
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Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**Pertussis Immunization; Family History of Convulsions  
and Use of Antipyretics — Supplementary ACIP Statement**

The Immunization Practices Advisory Committee (ACIP) has reviewed available data concerning the risks and benefits of pertussis vaccine for infants and children with a family history of convulsions. Based on this review, the ACIP does not believe that a family history of convulsions should be a contraindication to vaccination with diphtheria and tetanus toxoids and pertussis vaccine (DTP). In addition, the ACIP believes that antipyretic use in conjunction with DTP vaccination may be reasonable in children with personal or family histories of convulsions. Consequently, the following statement updates some of the previous recommendations regarding pertussis vaccine (1).

**Vaccination of Children with Family Histories of Convulsions with Pertussis Vaccine**

The risk of neurologic events after DTP vaccination is very small. Most neurologic events (primarily febrile seizures, but including nonfebrile seizures, encephalopathy, or other neurologic symptoms) that occasionally follow DTP vaccination occur in children without known risk factors. However, recent studies suggest that infants and children with a history of convulsions in first-degree family members (i.e., siblings and parents) have a 3.2-fold increased risk for neurologic events compared with those without such histories (CDC, unpublished data). Nevertheless, these children are still at very low risk for serious neurologic events following DTP vaccination. Convulsions within 3 days of DTP vaccination may be unrelated to vaccination, induced by vaccine components, or initiated by vaccine-associated fever in those children prone to febrile convulsions. Although children with a family history of seizures have an increased risk for developing idiopathic epilepsy, febrile seizures (including those following vaccinations) do not themselves increase the probability of epilepsy or other neurologic disorders (2,3).

After careful deliberation, the ACIP has concluded that a family history of convulsions in parents and siblings is not a contraindication to pertussis vaccination and that children with such family histories should receive pertussis vaccine according to the recommended schedule (1,4). The committee reached this decision after considering 1) the risks of pertussis disease, 2) the large number of children (5%-7%) with a family history of convulsions, 3) the clustering of these children within families, and 4) the low risk of convulsions following pertussis vaccination (1-3,5).

The ACIP believes that parents of infants and children with family histories of convulsions should be informed of their children's increased risk of seizures following DTP vaccination. In particular, they should be told, before the child is vaccinated, to seek immediate medical evaluation in the unlikely event of a seizure. The child's permanent medical record should document that the small risk of post-vaccination seizure and the benefits of pertussis vaccination have been discussed.

**Antipyretic Use in Children with Personal or Family Histories of Convulsions**

There are no data on whether the prophylactic use of antipyretics following DTP vaccine can decrease the risk of febrile convulsions. However, preliminary information suggests that acetaminophen given at a dose of 15 mg/kg at the time of DTP vaccination and again 4 hours later will reduce the incidence of postvaccination fever (6). Thus, it is reasonable to consider administering antipyretics (such as acetaminophen) at age-appropriate doses at the time of vaccination and every 4 to 6 hours for 48 to 72 hours to children at higher risk for seizures than the general population.

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# IMPORTANT INFORMATION ABOUT DIPHTHERIA, TETANUS, AND PERTUSSIS AND DTP, DT, AND Td VACCINES

*Please read this carefully*

DTP 1/1/88

## WHAT IS DIPHTHERIA?

Diphtheria is a very serious disease which can affect people in different ways. It can cause an infection in the nose and throat which can interfere with breathing. It can also cause an infection of the skin. Sometimes it causes heart failure or paralysis. About 1 person out of every 10 who get diphtheria dies of it.

## WHAT IS TETANUS?

Tetanus, or lockjaw, results when wounds are infected with tetanus bacteria, which are often found in dirt. The bacteria in the wound make a poison which causes the muscles of the body to go into spasm. In the United States, four out of every 10 persons who get tetanus die of it.

## WHAT IS PERTUSSIS?

Pertussis, or whooping cough, causes severe spells of coughing which can interfere with eating, drinking, and breathing. In the United States, approximately 70 percent of reported pertussis cases occur in children younger than 5 years. Pertussis is a more serious disease in young children and more than half of the children less than 1 year of age reported to have pertussis are hospitalized. In recent years, over 2,000 cases of pertussis have been reported each year in the United States. Complications occur in a substantial proportion of reported cases. Pneumonia occurs in one of every four children with pertussis. For every 1,000 reported pertussis cases, 22 develop convulsions and/or have more severe problems of the brain. In recent years, an average of nine deaths due to pertussis occurred annually.

Before vaccines were developed, these three diseases were all very common and caused a large number of deaths each year in the United States. If children are not immunized, the risk of getting these diseases will go back up again.

## DTP, DT, AND Td VACCINES:

Immunization with DTP vaccine is the best way to prevent these diseases. DTP vaccine is actually three vaccines combined into one shot to make it easier to get protection. Advisory committees of the United States Public

*(PLEASE READ OTHER SIDE)*

Health Service and the American Academy of Pediatrics recommend DTP vaccine be used in children up to their seventh birthday. The vaccine is given by injection starting early in infancy. At least three shots are needed to provide initial protection. Young children should get three doses in the first year of life and a fourth dose at about 15 months of age. A booster shot is important for children who are about to enter school and should be given between their fourth and seventh birthdays. The vaccine is very effective at preventing tetanus—over 95 percent of those who get the vaccine are protected if the recommended number of shots is given. Although the diphtheria and pertussis parts of the vaccine are not quite as effective, they still prevent most children from getting disease and they make the disease milder for those who do get it. Because pertussis is not very common or severe in older children, those 7 years of age or older should take a vaccine that does not contain the pertussis part. Also, because reactions to the diphtheria part of the vaccine may be more common in older children, those 7 years of age and older should take a form of the vaccine that has a lower concentration of the diphtheria part. This vaccine which contains no pertussis part and a lower concentration of the diphtheria part is called Td vaccine. Boosters with the Td vaccine should be received every 10 years throughout life.

## DEFERRAL OF DTP IMMUNIZATION:

Children who have had a serious reaction to previous DTP shots should not receive additional pertussis vaccine (see WARNING). A preparation called DT vaccine is available for them which does not contain the pertussis part. Also, children who have previously had a convulsion or are suspected to have a problem of the nervous system should not receive DTP vaccine until a full medical evaluation has been made.

## POSSIBLE SIDE EFFECTS FROM THE VACCINE:

With DTP vaccine, most children will have a slight fever and be irritable within 2 days after getting the shot. One-half of children develop some soreness and swelling in the area where the shot was given. More serious side effects can occur.

Forms provided by: Montana Immunization Program  
Dept. of Health & Environmental Sciences  
Helena, MT 59620

A temperature of 105°F or greater may follow 1 out of 330 DTP shots. Continuous crying lasting 3 or more hours may occur after 1 in every 100 shots and unusual, high-pitched crying may occur after 1 in every 900 shots. Convulsions or episodes of limpness and paleness may each occur after 1 in every 1,750 shots. Rarely, about once in every 110,000 shots, other more severe problems of the brain may occur, and permanent brain damage may occur about once in every 310,000 shots. Side effects from DT or Td vaccine are not common and usually consist only of soreness and slight fever. As with any drug or vaccine, there is a rare possibility that allergic or more serious reactions or even death could occur.

Although some people have questioned whether DTP shots might cause Sudden Infant Death Syndrome (SIDS), the majority of evidence indicates that DTP shots do not cause SIDS.

### PERSONAL OR FAMILY HISTORY OF CONVULSIONS:

Children who have had a convulsion and children who have a brother, sister, or parent who has ever had a convulsion are more likely to have a convulsion after receiving DTP vaccine. The advisory committees recommend that because of the overall risk of pertussis disease and the fact that the risk of convulsions is still very low: (1) children with a personal history of a convulsion and whose nervous system problem is stable may receive DTP vaccine; and (2) children with a family history of convulsions should receive DTP vaccine. However, you should tell the person who is to give the immunization about such a history and discuss the possibility of using an anti-fever medicine.

### PREGNANCY:

Babies born under unsanitary conditions to unimmunized women have a risk of developing tetanus during the newborn period (neonatal tetanus). Neonatal tetanus can be prevented by immunization of adult women. Women who have not received Td earlier and who are thought to be at risk of delivering their babies under unsanitary conditions should be immunized during pregnancy. Td vaccine is not known to cause special problems for pregnant women or their

unborn babies. Doctors usually do not recommend giving any drugs or vaccines to pregnant women unless there is a specific need. Pregnant women who need Td vaccine should receive it, preferably during the second and/or third trimesters.

### WARNING—SOME PERSONS SHOULD NOT TAKE THESE VACCINES WITHOUT CHECKING WITH A DOCTOR:

- Anyone who is sick right now with something more serious than a cold.
- Anyone who has had a convulsion or is suspected to have a problem of the nervous system.
- Anyone who has had a serious reaction to DTP, DT, or Td shots before, such as: an allergic reaction to any vaccine component; a temperature of 105°F or greater; an episode of limpness and paleness; prolonged continuous crying; an unusual, high-pitched cry; or a convulsion or other more severe problem of the brain.
- Anyone taking a drug or undergoing a treatment that lowers the body's resistance to infection, such as: cortisone, prednisone, certain anticancer drugs, or irradiation.
- Anyone who has had a serious reaction to a product containing thimerosal, a mercurial antiseptic.

### QUESTIONS:

If you have any questions about diphtheria, tetanus, or pertussis or DTP, DT, or Td immunization, please ask us now or call your doctor or health department before you sign this form.

### REACTIONS:

If the person who received the vaccine develops a temperature of 105°F or greater, continuous crying lasting 3 or more hours, an unusual high-pitched cry, a convulsion, an episode of limpness and paleness, or a severe problem of the brain, the person should be seen promptly by a doctor.

If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after immunization, please report it to:

### PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

*I have read or have had explained to me the information on this form about diphtheria, tetanus, and pertussis and DTP, DT and Td vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of the DTP, DT, and Td vaccine and request that the vaccine checked below be given to me or to the person named below for whom I am authorized to make this request.*

Vaccine to be given  DTP  DT  Td

DTP 1/1/88

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                                   |            |        |           |        | FOR CLINIC USE     |                       |
|--|------------|--------|-----------|--------|--------------------|-----------------------|
| Last Name  | First Name | MI     | Birthdate | Age    | Clinic Ident.      |                       |
| Address  |            |        |           |        | Date Vaccinated    |                       |
| City   |            | County |           | State  | Manuf. and Lot No. |                       |
| X<br>Signature of person to receive vaccine or person authorized to make the request.        |            |        |           |        | Date               |                       |
| FOR DATA PROCESSING USE ONLY (OPTIONAL)  |            |        |           |        |                    |                       |
| VACCINE HISTORY: PLACE CHECK <input type="checkbox"/> IN BOX IF HISTORY PREVIOUSLY SUBMITTED |            |        |           |        |                    |                       |
| DTP:   | m/d/yr     | m/d/yr | m/d/yr    | m/d/yr | m/d/yr             | MEASLES: m/d/yr       |
| POLIO:   | m/d/yr     | m/d/yr | m/d/yr    | m/d/yr | m/d/yr             | MUMPS: m/d/yr         |
|  |            |        |           |        | RUBELLA: m/d/yr    | HAEMOPHILUS b: m/d/yr |

INSTRUCTIONAL FOR DOSE RECOVERY FROM A VIAL OF DTP ABSORBED USP  
Developed by Connaught Laboratories, Inc.

1.0 Introduction

This procedure is intended for those persons requiring further instructions on how to recover the full 15 doses from a vial of Diphtheria and Tetanus Toxoids and Pertussis Vaccines Absorbed USP (DTP). This procedure defines the materials required as well as the methods to be used when withdrawing a dose of DTP from a multiple dose vial.

2.0 Sterile Materials:

- 2.1 DTP 7.5 ml vial
- 2.2 Luer Lock Syringe (maximum volume of 3 ml)
- 2.3 Needle (maximum size of 25G 5/8")
- 2.4 Alcohol preparation sponge

3.0 Withdrawal Methods

- 3.1 Remove the metal tab from the center of the cap enclosing the vial.
- 3.2 Swab the exposed portion of the rubber stopper with the alcohol preparation sponge.
- 3.3 Remove the syringe (maximum volume of 3 ml) from the sterile package. Peel back the sterile package enclosing the needle exposing the hub. Remove the protective cap from the luer lock end of the syringe and aseptically insert the hub of the needle into the luer lock of the syringe. Twist the needle and syringe in the opposite directions to ensure that they don't come apart.
- 3.4 Remove the protective cap from the needle and pull the barrel back to the 0.5 ml graduation on the syringe.
- 3.5 Insert the needle through the rubber stopper into the vial.
- 3.6 Invert the vial to avoid withdrawal of air and withdraw 0.5 ml of product from the vial.
- 3.7 Return the vial to the upright position and withdraw the needle from the stopper. (This will avoid potential for product loss that could be experienced if the vial in the inverted position).
- 3.8 Refer to DTP product insert under Dosage and Administration for further instructions.



# Optimum Needle Length for Diphtheria-Tetanus-Pertussis Inoculation of Infants

There is no consensus about the most appropriate needle length for injection of diphtheria-tetanus-pertussis (DTP) vaccine in infants. IM administration with a 2.54 to 3.17 cm (1- to 1¼-in) needle was recommended according to the 1982 Red Book.<sup>1</sup> A specific recommendation for needle length was deleted from the 1986 Red Book,<sup>2</sup> although IM administration was still recommended. This route is preferred because of the known risk of sterile abscess formation related to subcutaneous administration of the DTP vaccine.<sup>3,4</sup>

No systematic surveys have been conducted among practitioners to establish the most commonly used needle length for DTP shots. We informally surveyed the five largest pediatric clinics in the Minneapolis-St Paul area and found that four of five clinics used a 1.58-cm (¾-in) needle.

To make a recommendation for needle length for IM injections on an objective basis, we studied the depth of the fat layer over the anterolateral thigh of infants using high-frequency, real-time ultrasonography.

## MATERIALS AND METHODS

We chose 4-month-old infants attending the well-child clinic at the Mayo Clinic for study. Exclusion criteria were a birth weight less than 2500 g, a major birth defect, and age younger than 3½ months or older than 4½ months. At the time of the 4-month-old examination, an attempt was made with informed consent to enroll every fourth infant boy and every fourth infant girl in the study, for a total of 13 boys and 11 girls.

The ultrasound instrument (Diasonics, Inc, Milpitas, CA) uses a 10-MHz frequency, which has a theoretical axial resolution of 0.5 mm.<sup>6</sup> Measurements were obtained at a point equidistant from the right anterior iliac crest and the superior border of the right patella, in the midline. The ultrasound transducer was lightly applied to the skin to avoid tissue compression. Skin to muscle measurements were obtained in the longitudinal plane, and skin to bone measurements were obtained in the trans-

verse plane. Two measurements were taken in each plane and averaged.

## RESULTS

For the 4-month-old infant boys, the skin to muscle depth (mean  $\pm$  SD) was 1.4  $\pm$  0.24 cm, and the skin to bone depth (mean  $\pm$  SD) was 3.2  $\pm$  0.45 cm. For the 4-month-old girls, the skin to muscle depth (mean  $\pm$  SD) was 1.3  $\pm$  0.28 cm and the mean skin to bone depth (mean  $\pm$  SD) was 2.8  $\pm$  0.47 cm.

## DISCUSSION

In a comprehensive review<sup>7</sup> of IM injection techniques it was recommended that such injections be given to infants in the anterolateral thigh. A 2.54-cm (1-in) needle is recommended for this purpose, with the needle tilted at a 45° angle to the long axis of the leg (Fig 1).

The rationale for these recommendations derives from the singular case report<sup>8</sup> of a 3-month-old infant in whom gangrene of the foot developed after IM administration of penicillin at a 90° angle to the long axis of the leg with a 3.81-cm (1½-in) needle. Although the injection was given in the anterolateral thigh, the femoral artery (which lies anteromedial to the femur) was compromised.

If a 1.58-cm (¾-in) needle is thrust into the thigh at a 45° angle, then the actual depth of penetration would be 1.12 cm (Fig 2). For our study population of 4-month-old infants, the muscle layer would have been penetrated in only 5 (21%) of the 24 subjects. According to the Ten-State Nutrition Survey,<sup>9</sup> there is no significant sex difference in fat-fold thickness at this age. In our study, the fat layer in

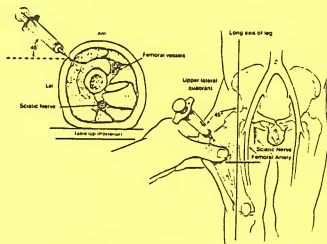


Fig 1. Suggested injection technique for anterior lateral thigh. (From Bergeson et al;<sup>7</sup> reproduced by permission of Pediatrics.)

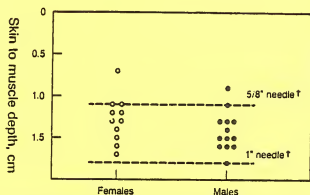


Fig 2. Thickness of anterolateral thigh fat layer in 4-month-old infants and depth of penetration at 45° angle.

infant boys was thicker than that in infant girls, but the sample is too small for this difference to be considered statistically significant. If, therefore, all 24 subjects are regarded as a homogeneous group, the 95% confidence interval for penetration to muscle by a 1.58-cm (5/8-in) needle at a 45° angle would be 7% to 42%. In contrast, the muscle layer would have been penetrated in all study infants by a 2.54-cm (1-in) needle at a 45° angle.

An argument could be made that it is safe to deliver IM shots in the anterolateral thigh of infants with a 1.56-cm (5/8-in) needle at a 90° angle to the longitudinal axis of the leg, but the objection to this viewpoint is that the muscle layer would not be penetrated in a significant number of infants. In this study, IM penetration would not have occurred in 25% of the study participants.

With a 2.54-cm (1-in) needle, there might be concern that the needle would at times strike the femur. With reference to the skin to bone depth of our study participants, this theoretically would not have occurred in any subject. In 2-month-old infants, manually bunching the tissue at the injection site in the recommended fashion<sup>7</sup> would increase muscle depth and minimize the chance of striking bone. Our nurses report that striking the femur with the 2.54-cm (1-in) needle is an exceptional event, even in 2-month-old infants.

For premature newborns at the first DTP vaccination and for newborn infants in general, individ-

ual discretion should be exercised in selecting a needle length for IM injections.

In our well-child clinic, we had used the 1.58-cm (5/8-in) needle routinely for DTP immunizations to infants for several years and had been concerned about the occasional but regular occurrence of sterile abscesses at the injection site. During the first year after changing to 2.54-cm (1-in) needles (23-gauge), we were aware of no cases of chronic nodules at the injection site and none could be identified by chart review.

In summary, measurement of the depth of the anterior thigh fat pad in 4-month-old infants by ultrasonography upholds previous recommendations that a 2.54-cm (1-in) needle is the preferred needle length for IM injections of infants.

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Poliomyelitis

VACCINE AVAILABILITY

Three types of poliovirus vaccines are currently licensed in the United States:

- Oral Polio Vaccine (OPV)
- Inactivated Polio Vaccine (IPV)
- Enhanced-Potency Inactivated Polio Vaccine

OPV supplied by the Immunization Program is currently supplied in single-dose units; each dose consists of 0.5 ml of trivalent vaccine.

IPV is indicated for individuals who, due to medical condition, should not receive OPV including persons with altered immune status due to certain diseases or due to immunosuppressive therapy. The Montana Immunization Program does not supply IPV but may be aware of clinics who do stock it.

See the attached ACIP statement and Important Information Form. Also refer to the Adult Immunization Recommendations on Poliomyelitis and the Control of Communicable Diseases in Man.



Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**Poliomyelitis Prevention**

*This revised ACIP recommendation on poliomyelitis prevention addresses issues important in poliomyelitis control in the United States today. Specifically, situations that constitute increased risk are defined, and alternatives for protection are outlined. Recommendations for immunization of adults are presented, clarifying the role of inactivated polio vaccine in immunizing adults. These recommendations also address the problems of interrupted immunization schedules and completion of primary immunization. Oral polio vaccine remains the vaccine of choice for primary immunization of children.*

**INTRODUCTION**

Poliovirus vaccines, used widely since 1955, have dramatically reduced the incidence of poliomyelitis in the United States. The annual number of reported cases of paralytic disease declined from more than 18,000 in 1954 to an average annual number of less than 13 in 1973-1980. The risk of poliomyelitis is generally very small in the United States today, but epidemics are likely to occur if the immunity of the population is not maintained by immunizing children beginning in the first year of life. Small outbreaks have occurred in 1970, 1972, and 1979 as a result of introduction of virus into susceptible populations in communities with low immunization levels.

As a result of the Childhood Immunization Initiative efforts 1977-1979, immunization levels in children are now higher than ever before. The School Enterer Assessments in kindergarten and first-grade levels have indicated that the percentage of these children who have completed primary vaccination against poliomyelitis reached 95% in the 1980-1981 school year. Immunization levels in preschool children and in those who are in higher grades may be substantially lower than the levels at school entry.

Laboratory surveillance of enteroviruses shows that the circulation of wild polioviruses has diminished markedly. Inapparent infection with wild strains no longer contributes significantly to establishing or maintaining immunity, making universal vaccination of infants and children even more important.

**POLIOVIRUS VACCINES**

Two types of poliovirus vaccines are currently licensed in the United States: Oral Polio Vaccine (OPV)\* and Inactivated Polio Vaccine (IPV).†

**Oral Polio Vaccine (OPV)**

Within several years after it was licensed in the United States in 1963, trivalent OPV, the live attenuated vaccine combining all 3 strains of poliovirus, almost totally supplanted the individual monovalent OPV antigens used earlier. Full primary vaccination with OPV will produce long-lasting immunity to all 3 poliovirus types in more than 95% of recipients. Most recipients are protected after a single dose.

OPV consistently induces intestinal immunity that provides resistance to reinfection with polioviruses. Administration of OPV may interfere with simultaneous infection by wild polioviruses, a property which is of special value in epidemic-control campaigns. In rare instances (once in approximately 3.2 million doses distributed), OPV has been associated with paralytic disease in vaccine recipients or their close contacts. In the 12-year period 1969-1980, approximately 290 million doses of OPV were distributed, and 92 cases of paralysis associated with vaccine were reported. Twenty-five cases of paralysis occurred in otherwise healthy vaccine recipients, 55 cases in healthy close contacts of vaccine recipients, and 12 cases in persons (recipients or contacts) with immune-deficiency conditions.

**Inactivated Polio Vaccine (IPV)**

Licensed in 1955, IPV has been used extensively in this country and many other parts of the world. It is given by subcutaneous injection. Where extensively used, IPV has brought about a great reduction in paralytic poliomyelitis cases. Approximately 428 million doses have been administered in the United States, mostly before

\*Official name: Poliovirus Vaccine, Live, Oral, Trivalent.

†Official name: Poliomyelitis Vaccine

1962. Although IPV has not been widely used in this country for more than a decade, a Canadian product licensed for use in the United States is now available.

It is generally accepted that primary vaccination with 4 doses of IPV produces immunity to all 3 poliovirus types in more than 95% of recipients. Additional experience with the IPV product available since 1968 is necessary to establish whether the duration of immunity is comparable to that induced by OPV. Experience in other countries forms the basis for the present recommendations on booster doses.

There is considerable evidence from epidemiologic studies that immunizing with IPV diminishes circulation of wild poliovirus in the community, although it is known that persons vaccinated with IPV can subsequently be infected with and excrete in feces either wild strains or attenuated vaccine virus strains. No paralytic reactions to IPV are known to have occurred since the 1955 cluster of poliomyelitis cases caused by vaccine that contained live polioviruses that had escaped inactivation. Serious adverse reactions are not anticipated with the current IPV product.

An improved IPV product with higher potency has been developed in Europe. Studies in Africa and Europe have revealed essentially 100% seroconversion following 2 doses. Duration of protection is under study. Preliminary studies are now under way in a U.S. population to compare this product with OPV.

## **ROUTINE IMMUNIZATION**

### **Rationale for Choice of Vaccine**

Although IPV and OPV are both effective in preventing poliomyelitis, OPV is the vaccine of choice for primary immunization of children in the United States when the benefits and risks for the entire population are considered. OPV is preferred because it induces intestinal immunity, is simple to administer, is well accepted by patients, results in immunization of some contacts of vaccinated persons, and has a record of having essentially eliminated disease associated with wild polioviruses in this country. The choice of OPV as the preferred polio vaccine in the United States has also been made by the Committee on Infectious Diseases of the American Academy of Pediatrics (1) and a special expert committee of the Institute of Medicine, National Academy of Sciences (2).

Some poliomyelitis experts contend that greater use of IPV in the United States for routine vaccination would provide continued control of naturally occurring poliovirus infections and simultaneously reduce the problem of OPV-associated disease. They argue that there is no substantial evidence that OPV and currently available IPV differ in their ability to protect individuals from disease. They question the public health significance of higher levels of gastrointestinal immunity achieved with OPV, and they question whether the transmission of vaccine virus to close contacts contributes substantially to the level of immunity achieved in the community.

Some countries successfully prevent poliomyelitis with IPV. However, because of many differences between these countries and the United States, particularly with respect to risks of exposure to wild polioviruses and the ability to achieve and maintain very high vaccination rates in the population, their experiences with IPV may not be directly applicable here.

Prospective vaccinees or their parents should be made aware of the polio vaccines available and the reasons why recommendations are made for giving specific vaccines at particular ages and under certain circumstances. Furthermore, the benefits and risks of the vaccines for individuals and the community should be stated so that vaccination is carried out among persons who are fully informed.

## **RECOMMENDATIONS FOR INFANTS, CHILDREN, AND ADOLESCENTS**

### **Primary Immunization (Table 1)**

**OPV:** For infants, children, and adolescents through secondary school age (generally up to age 18) the primary series of OPV consists of 3 doses. In infancy the primary series is integrated with DTP vaccination, and the first dose is commonly given at 6-12 weeks of age. At all ages the first 2 doses should be separated by at least 6, and preferably 8, weeks. The third dose is given at least 6 weeks, customarily 8-12 months, after the second dose. In high-risk areas, an additional dose of OPV is often given within the first 6 months of life. Breast feeding does not interfere with successful immunization.

**IPV:** The primary series consists of 4 doses of vaccine; volume and route of injection are specified by the manufacturer. In infancy, the primary schedule is usually integrated with DTP vaccination, as with OPV. Three doses can be given at 4- to 8-week intervals; the fourth dose should follow 6-12 months after the third.

All children should complete primary immunization before entering school, preferably with all OPV or all IPV. If, however, a combination of IPV and OPV is used, a total of 4 doses constitutes a primary series.

### **Supplementary Immunization**

**OPV:** Before entering school, all children who previously received primary immunization with OPV (3 doses) in early childhood should be given a fourth dose. However, if the third primary dose is administered on or after

the fourth birthday, a fourth (supplementary) dose is not required. The additional dose will increase the likelihood of complete immunity in the small percentage of children who have not previously developed serum antibodies to all 3 types of polioviruses. The need for supplementary doses after 4 doses of OPV has not been established, but children considered to be at increased risk of exposure to poliovirus (as noted below under **RECOMMENDATIONS FOR ADULTS**) may be given a single additional dose of OPV.

*IPV:* Before entering school, all children who previously received primary immunization with either IPV alone or a combination of IPV and OPV (a total of 4 doses) in early childhood should be given at least 1 dose of OPV or 1 additional dose of IPV. However, if the fourth primary dose is administered on or after the fourth birthday, a fifth (supplementary) dose is not required at school entry. Use of a primary series of OPV would eliminate the need for subsequent booster doses of IPV. Children who received primary immunization with IPV should obtain a booster dose of IPV every 5 years until the age of 18 years, unless a primary series of OPV is given. The need for such supplementary doses after the 5 basic doses of the currently available IPV product has not been firmly established. Further experience may lead to alteration of this recommendation.

#### Children Incompletely Immunized

Polio vaccination status should be reevaluated periodically, and those who are inadequately protected should complete their immunizations.

*OPV:* To help assure seroconversion to all 3 serotypes of poliovirus, completion of the primary series of 3 doses of OPV is recommended. Time intervals between doses longer than those recommended for routine primary immunization do not necessitate additional doses of vaccine. Individuals who received only 1 dose of each of the monovalent OPVs in the past should receive 2 doses of trivalent OPV at least 6 weeks apart. One dose of each monovalent OPV (poliovirus types 1, 2, and 3) is at least equivalent to 1 dose of trivalent OPV.

*IPV:* Regulations for vaccine licensure adopted since 1968 require a higher potency IPV than was previously manufactured. Four doses of IPV administered after 1968 are considered a complete primary series. As with

**TABLE 1. Routine poliomyelitis immunization schedule summary, 1981\***

| Dose                     | OPV<br>age/interval                                    | IPV<br>age/interval                             |
|--------------------------|--|---|
| Primary 1                | Initial visit, preferably<br>6-12 weeks of age         | Initial visit, preferably<br>6-12 weeks of age  |
| Primary 2                | Interval of 6-8 weeks                                  | Interval of 4-8 weeks                           |
| Primary 3                | Interval of $\geq 6$ weeks,<br>customarily 8-12 months | Interval of 4-8 weeks                           |
| Primary 4                |  | Interval of 6-12 months                         |
| Supplementary            | 4-6 years of age <sup>†</sup><br>(school entry)        | 4-6 years of age <sup>†</sup><br>(school entry) |
| Additional supplementary |  | Interval of every 5 years <sup>§</sup>          |

\*Important details are in the text.

<sup>†</sup>If the third primary dose of OPV is administered on or after the fourth birthday, a fourth (supplementary) dose is not required. If the fourth primary dose of IPV is administered on or after the fourth birthday, a fifth (supplementary) dose is not required at school entry.

<sup>§</sup>Supplementary doses are recommended every 5 years after the last dose until the 18th birthday or unless a complete primary series of OPV has been completed.

OPV, time intervals between doses longer than those recommended for routine primary immunization do not necessitate additional doses.

Incompletely immunized children who are at increased risk of exposure to poliovirus (as noted below under **RECOMMENDATIONS FOR ADULTS**) should be given the remaining required dose or, if time is a limiting factor, at least a single dose of OPV.

#### **RECOMMENDATIONS FOR ADULTS**

Routine primary poliovirus vaccination of adults (generally those 18 years old or older) residing in the United States is not necessary. Most adults are already immune and also have a very small risk of exposure to poliomyelitis in the United States. Immunization is recommended for certain adults who are at greater risk of exposure to wild polioviruses than the general population, including:

1. travelers to areas or countries where poliomyelitis is epidemic or endemic;
2. members of communities or specific population groups with disease caused by wild polioviruses;
3. laboratory workers handling specimens which may contain polioviruses;
4. health-care workers in close contact with patients who may be excreting polioviruses.

For individuals in the above categories, polio vaccination is recommended as detailed below.

#### **Unvaccinated Adults**

For adults at increased risk of exposure to poliomyelitis, primary immunization with IPV is recommended whenever this is feasible. IPV is preferred because the risk of vaccine-associated paralysis following OPV is slightly higher in adults than in children. Three doses should be given at intervals of 1-2 months; a fourth dose should follow 6-12 months after the third.

In circumstances where time will not allow at least 3 doses of IPV to be given before protection is required, the following alternatives are recommended:

1. If less than 8, but more than 4, weeks are available before protection is needed, 2 doses of IPV should be given at least 4 weeks apart.
2. If less than 4 weeks are available before protection is needed, a single dose of OPV is recommended.

In both instances, the remaining doses of vaccine should be given later at the recommended intervals, if the person remains at increased risk.

#### **Incompletely Immunized Adults**

Adults who are at increased risk of exposure to poliomyelitis and who have previously received less than a full primary course of OPV or IPV should be given the remaining required doses of either vaccine, regardless of the interval since the last dose and the type of vaccine previously received.

#### **Adults Previously Given a Complete Primary Course of OPV or IPV**

Adults who are at increased risk of exposure to poliomyelitis and who have previously completed a primary course of OPV may be given another dose of OPV. The need for further supplementary doses has not been established. Those adults who previously completed a primary course of IPV may be given a dose of either IPV or OPV. If IPV is used exclusively, additional doses may be given every 5 years, but their need also has not been established.

#### **UNIMMUNIZED OR INADEQUATELY IMMUNIZED ADULTS IN HOUSEHOLDS IN WHICH CHILDREN ARE TO BE GIVEN OPV**

Adults who have not been adequately immunized against poliomyelitis with OPV or IPV are at a very small risk of developing OPV-associated paralytic poliomyelitis when children in the household are given OPV. About 4 such cases have occurred annually among contacts since 1969, during which time about 24 million doses of OPV were distributed yearly. (See **ADVERSE REACTIONS**.)

Because of the overriding importance of ensuring prompt and complete immunization of the child and the extreme rarity of OPV-associated disease in contacts, the Committee recommends the administration of OPV to a child regardless of the poliovirus-vaccine status of adult household contacts. This is the usual practice in the United States. The responsible adult should be informed of the small risk involved. An acceptable alternative, if there is strong assurance that ultimate, full immunization of the child will not be jeopardized or unduly delayed, is to immunize adults according to the schedule outlined above before giving OPV to the child.

#### **PRECAUTIONS AND CONTRAINDICATIONS**

##### **Pregnancy**

Although there is no convincing evidence documenting adverse effects of either OPV or IPV on the pregnant woman or developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women. However, if immediate protection against poliomyelitis is needed, OPV is recommended.

## Immunodeficiency

Patients with immune-deficiency diseases, such as combined immunodeficiency, hypogammaglobulinemia and agammaglobulinemia, should not be given OPV because of their substantially increased risk of vaccine-associated disease. Furthermore, patients with altered immune states due to diseases such as leukemia, lymphoma, or generalized malignancy, or with immune systems compromised by therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation should not receive OPV because of the theoretical risk of paralytic disease. OPV should not be used for immunizing immunodeficient patients and their household contacts; IPV is recommended. Many immunosuppressed patients will be immune to polioviruses by virtue of previous immunization or exposure to wild-type virus at a time when they were immunologically competent. Although these persons should not receive OPV, their risk of paralytic disease is thought to be less than that of naturally immunodeficient individuals. Although a protective immune response to IPV in the immunodeficient patient cannot be assured, the vaccine is safe and some protection may result from its administration. If OPV is inadvertently administered to a household-type contact of an immunodeficient patient, close contact between the patient and the recipient of OPV should be avoided for approximately 1 month after vaccination. This is the period of maximum excretion of vaccine virus. Because of the possibility of immunodeficiency in other children born to a family in which there has been 1 such case, OPV should not be given to a member of a household in which there is a family history of immunodeficiency until the immune status of the recipient and other children in the family is documented.

## ADVERSE REACTIONS

### OPV

In rare instances, administration of OPV has been associated with paralysis in healthy recipients and their contacts. Other than efforts to identify persons with immune-deficiency conditions, no procedures are currently available for identifying persons likely to experience such adverse reactions. Although the risk of vaccine-associated paralysis is extremely small for vaccinees and their susceptible, close, personal contacts, they should be informed of this risk.

### IPV

No serious side effects of currently available IPV have been documented. Since IPV contains trace amounts of streptomycin and neomycin, there is a possibility of hypersensitivity reactions in individuals sensitive to these antibiotics.

## CASE INVESTIGATION AND EPIDEMIC CONTROL

Each suspected case of poliomyelitis should prompt an immediate epidemiologic investigation, including an active search for other cases. If evidence implicates wild poliovirus and there is a possibility of transmission, a vaccination plan designed to contain spread should be developed. If evidence implicates vaccine-derived poliovirus, no vaccination plan need be developed, as no outbreaks associated with vaccine virus have been documented to date. Within an epidemic area, OPV should be provided for all persons over 6 weeks of age who have not been completely immunized or whose immunization status is unknown, with the exceptions noted above under Immunodeficiency.

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This recommendation supersedes the recommendation on poliomyelitis published in *MMWR* 1979;28:510-20.

Polio  
(1/82)





Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Poliomyelitis Prevention: Enhanced-Potency Inactivated Poliomyelitis Vaccine –  
Supplementary Statement**

The supplementary statement provides information on and recommendations for the use of inactivated poliovirus vaccine (IPV) of enhanced potency.\* The Immunization Practices Advisory Committee (ACIP) believes that, in the United States, polio immunization should rely primarily on oral poliovirus vaccine (OPV), with selected use of enhanced-potency IPV as specified in this document. However, this subject should be reviewed on a continuing basis, and an extensive review of polio vaccines and potential vaccine policies will take place during 1988. General recommendations on poliomyelitis prevention, including the use of and schedules for OPV, are found in the current ACIP recommendations (1).

**Introduction**

*Conventional IPV.* IPV was introduced in the United States in 1955 and was used widely until OPV became available during the period 1961-1964. Thereafter, the use of IPV rapidly declined to a level of less than 1% of all polio vaccine distributed annually in the United States.

In recent U.S. studies, three doses of IPV administered in the first year of life produced antibodies to poliovirus serotypes 1, 2, and 3 in 87%, 97%, and 95% of recipients, respectively. More than 99% of children completing the four-dose primary series by 18 months of age produced antibodies to all three serotypes (2).

*Enhanced-Potency IPV.* A method of producing a more potent IPV with greater antigenic content was developed in 1978 and led to the newly licensed IPV, which is produced in human diploid cells (3). Results of studies from several countries have indicated that a reduced number of doses of IPV produced with this technique can immunize children satisfactorily (4-6). A clinical trial of two preparations of enhanced-potency IPV was completed in the United States in 1984 (7). Children received three doses of one of the enhanced-potency IPV's at 2, 4, and 18 months of age. In spite of the presence of maternal antibodies in the majority of the infants at the time of the first dose, 99%-100% of the children were seropositive for all three poliovirus types at 6 months of age (2 months after their second dose). The percentage of seropositive children did not rise or fall significantly during the 14-month period following the second dose, a result that confirms that seroconversion had occurred in almost all children. Furthermore, geometric mean titers increased 5- to 10-fold following both the second and third doses. Conclusive studies are not yet available concerning antibody persistence following three doses of the enhanced-potency IPV to be made available in the United States. However, unpublished studies of an IPV with lower antigen content have shown 100% seropositivity 5 years after the third dose (2).

The effect of enhanced-potency IPV on the circulation of poliovirus in a community has not yet been determined, but it is likely to be at least as good as that seen with conventional IPV. In a recent study of poliovirus excretion following type 1 vaccine-virus challenge after the third dose of enhanced-potency IPV, the decrease in excretion was at least as great as that after conventional IPV, but still significantly less than that found after three doses of OPV (8).

**Vaccine Usage**

*Indications.* Persons with a congenital immune deficiency disease, such as agammaglobulinemia; an acquired immune deficiency disease, such as acquired immunodeficiency syndrome (AIDS); or an altered immune status as a result of other diseases or immunosuppressive therapy are at increased risk for paralysis associated with OPV. Therefore, if polio immunization is indicated, these persons and

\*Poliovirus Vaccine Inactivated, which is manufactured by Connaught Laboratories Ltd., will be distributed by Connaught Laboratories Inc. beginning in March 1988.

their household members and other close contacts should receive IPV rather than OPV. Although a protective immune response following receipt of enhanced-potency IPV cannot be assured, some protection may be provided to the immunocompromised patient. Available data on children previously diagnosed with asymptomatic human immunodeficiency virus (HIV) infection do not suggest that they are at increased risk of adverse consequences from OPV. However, for such persons, use of IPV rather than OPV is prudent since family members may be immunocompromised because of AIDS or HIV infection and may be at increased risk for paralysis from contact with an OPV virus.

Routine primary poliovirus vaccination of adults (generally those 18 years of age or older) residing in the United States is not recommended. Adults at increased risk of exposure to either vaccine or wild poliovirus (1) should receive polio vaccination in accordance with the schedule prescribed below.

In households where polio vaccine is to be administered to immunologically normal children, ACIP recommends giving OPV regardless of the poliovirus-vaccine status of adult household contacts (1). The overall risk of vaccine-associated paralytic disease in immunologically normal contacts of OPV recipients is one case per 5.5 million doses of OPV distributed (9). As an alternative, adult contacts can first complete their primary series of polio vaccine as detailed in the schedule below, if there is strong assurance that subsequent immunization of the child will not be jeopardized or unduly delayed.

*Schedules.* The primary series for enhanced-potency IPV consists of three 0.5-ml doses administered subcutaneously. The interval between the first two doses should be at least 4 weeks, but preferably 8 weeks. The third dose should follow in at least 6 months, but preferably nearer to 12 months. A primary series can be started as early as 6 weeks of age, but preferably at 2 months of age. Although studies have not been conducted, young children should receive the third dose along with diphtheria, tetanus, pertussis vaccine (DTP) and measles, mumps, rubella vaccine (MMR) at 15 months of age, if possible.

A primary series of polio vaccine usually consists of enhanced-potency IPV alone or OPV alone. However, a combination of both vaccines totalling three doses and separated by appropriate intervals constitutes a primary series. If enhanced-potency IPV is administered to persons with a previously incomplete series of conventional IPV, a final total of four doses of polio vaccine is necessary for a primary series.

All children who received a primary series of enhanced-potency IPV or of a combination of polio vaccines should be given a booster dose before entering school, unless the final dose of the primary series was administered on or after the fourth birthday. The need for routinely administering additional doses is unknown at this time.

For unvaccinated adults at increased risk of exposure to poliovirus, a primary series of enhanced-potency IPV is recommended. While the responses of adults to a primary series have not been studied, the recommended schedule for adults is two doses given at a 1- to 2-month interval and a third dose given 6 to 12 months later. If less than 3 months but more than 2 months are available before protection is needed, three doses of enhanced-potency IPV should be given at least 1 month apart. Likewise, if only 1 to 2 months are available, two doses of enhanced-potency IPV should be given at least 1 month apart. If less than 1 month is available, a single dose of either OPV or enhanced-potency IPV is recommended.

Adults who are at increased risk of exposure and have had 1) at least one dose of OPV, 2) fewer than three doses of conventional IPV, or 3) a combination of conventional IPV and OPV totalling fewer than three doses should receive at least one dose of OPV or enhanced-potency IPV. Additional doses needed to complete a primary series should be given if time permits.

Adults who are at increased risk of exposure and who have previously completed a primary series with any one or combination of polio vaccines can be given a dose of OPV or enhanced-potency IPV.

*Side Effects and Adverse Reactions.* Available data indicate that the rate of adverse reactions in the kidney cells of monkeys receiving enhanced-potency IPV are low and that the reactions are not different from those following administration of a placebo. The recently licensed human diploid cell-derived vaccine was not compared to a placebo. Rates of local adverse events following its use are similar to rates found in controlled studies using vaccine derived from the kidney cells of monkeys. There is no evidence that conventional IPV causes any serious side effects. Consequently, serious side effects are not expected to occur with enhanced-potency IPV. This conclusion can be confirmed only with postmarketing surveillance. Parents of children receiving the vaccine, older vaccine recipients, and health-care providers are encouraged to report all adverse events occurring within 4 weeks of receipt of enhanced-potency IPV to the manufacturer and to local or state health departments. The

information will be forwarded to the appropriate federal agency.<sup>†</sup>

**Precautions and Contraindications.** Vaccine administration should not be postponed because of minor illnesses, such as mild upper-respiratory infections. Generally, however, persons with severe febrile illnesses should not be vaccinated until they have recovered.

The enhanced-potency IPV may contain trace amounts of streptomycin and neomycin. Persons who have had anaphylactic reactions to topically or systemically administered streptomycin and neomycin should not receive enhanced-potency IPV.

There is no convincing evidence documenting adverse effects of conventional IPV on the pregnant woman or developing fetus. Data on adverse events following use of enhanced-potency IPV are not available. On theoretical grounds, it is prudent to avoid vaccinating pregnant women. However, if a pregnant woman needs immediate protection against poliomyelitis, OPV is recommended.

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<sup>†</sup>Center for Biologics Evaluation and Research, Food and Drug Administration, or the Centers for Disease Control.



# IMPORTANT INFORMATION ABOUT POLIO AND ORAL POLIO VACCINE

*Please read this carefully*

OP 3/1/83

**WHAT IS POLIO?** Polio is a virus disease that may cause permanent crippling (paralysis) and occasionally death. There used to be thousands of cases and hundreds of deaths from polio every year in the United States. Because of the widespread use of polio vaccines, which became available beginning in the mid-1950's, polio disease has nearly been eliminated from the United States. Although thousands of cases continue to occur each year in the rest of the world, in the United States during the past 5 years there have been only 67 cases of polio reported, an average of 13 cases per year. Our success in preventing the spread of wild polio virus has been so great that most of the recent cases (approximately nine per year) have resulted from the rare side effects of oral polio vaccine (see below). Because of this fact, some people have asked why we should continue to use polio vaccine. The reason is that, even though we may not have much wild polio virus spreading here now, there is so much of it in the rest of the world that there is a great risk of its being reestablished if our children are not vaccinated.

**ORAL LIVE POLIO VACCINE:** Immunization with oral live polio vaccine (OPV) is one of the best ways to prevent polio. It is given by mouth starting in early infancy. Several doses are needed to provide good protection. Young children should get two or more doses in the first year of life and another dose at about 18 months of age. An additional dose is important for children when they enter school or when

there is a high risk of polio, for example, during an epidemic or when traveling to a place where polio is common. The vaccine is easy to take and is effective in preventing the spread of polio. In over 90 percent of people, OPV gives protection for a long time, probably for life. Because OPV viruses live for a time in the intestinal tract of the person who is vaccinated, some of the viruses pass in the stool and can spread from the vaccinated person to those in close contact (usually household members). This may help to immunize these persons and is one of the advantages of OPV. The Immunization Practices Advisory Committee of the Public Health Service and the American Academy of Pediatrics recommend oral live polio vaccine as the preferred polio vaccine for people up to the 18th birthday.

**POSSIBLE SIDE EFFECTS FROM THE VACCINE:** OPV very rarely (once in about every 8.1 million doses of OPV distributed) causes paralytic polio in the person who is vaccinated. The risk may be slightly higher in adults being vaccinated and substantially higher in persons with abnormally low resistance to infection. Also very rarely (once in about every 5 million doses of OPV distributed) paralytic polio may develop in a close contact of a recently vaccinated person. Even though these risks are very low, they should be recognized. The risk of side effects from the vaccine must be balanced against the risk of the disease, both now and in the future.

*(PLEASE READ OTHER SIDE)*

Forms provided by: MONTANA DEPARTMENT OF HEALTH AND ENVIRONMENTAL SCIENCES  
Childhood Immunization Program  
Cogswell Building  
Helena, MT 59620

**PREGNANCY:** Polio vaccine experts do not think oral polio vaccine can cause special problems for pregnant women or their unborn babies. However, doctors usually avoid giving any drugs or vaccines to pregnant women unless there is a specific need. Pregnant women should check with a doctor before taking oral polio vaccine.

**WARNING—SOME PERSONS SHOULD NOT TAKE ORAL POLIO VACCINE WITHOUT CHECKING WITH A DOCTOR:**

- Anyone with cancer, leukemia, or lymphoma.
- Anyone with a disease that lowers the body's resistance to infection.
- Anyone taking a drug that lowers the body's resistance to infection, such as cortisone or prednisone.
- Anyone who lives in the same household with anyone who has one of the conditions listed above.
- Anyone who is sick right now with something more serious than a cold.
- Pregnant women.
- Most persons age 18 and older because adults have a slightly bigger risk of developing paralysis from oral polio vaccine than children (However, if the risk of polio is increased—as may occur, for example, when there is an outbreak in your community—most polio experts recommend that unprotected persons receive oral polio vaccine regardless of age.)

**NOTE ON INJECTABLE (KILLED) POLIO VACCINE:**

Besides the oral polio vaccine (OPV), there is also a killed polio vaccine (IPV) given by injection which protects against

polio after several shots. This killed polio vaccine has no known risk of causing paralytic polio. Because OPV may provide lifetime protection, seems to provide stronger immunity in the intestinal tract (where infection first occurs), is simpler to administer, and is more effective in preventing the spread of polio virus than IPV, most polio experts feel that oral vaccine is more effective for controlling polio in the United States. Injectable polio vaccine is recommended for persons needing polio vaccination who have low resistance to serious infections or who live with persons with low resistance to serious infections. It may also be recommended for previously unvaccinated adults who plan to travel to a place where polio is common or for previously unvaccinated adults whose children are to be vaccinated with OPV. It is not widely used in this country at the present time, but it is available. If you would like to know more about this type of polio vaccine, or wish to receive this vaccine, please ask us.

**QUESTIONS:** If you have any questions about polio or polio vaccination, please ask us now or call your doctor or health department before you sign this form.

**REACTIONS:** If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after vaccination, please report it to:

**PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS**

*I have read the information on this form about polio and the oral vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of oral polio vaccine and request that it be given to me or to the person named below for whom I am authorized to make this request.*

OP 3/1/83

| INFORMATION ON PERSON TO RECEIVE VACCINE (Please Print)                          |            |       |           |      |
|--|------------|-------|-----------|------|
| Last Name  | First Name | MI    | Birthdate | Age  |
| Address  |            |       |           |      |
| City   | County     | State | Zip       |      |
| X  |            |       |           | Date |
| Signature of person to receive vaccine or person authorized to make the request. |            |       |           |      |

| FOR CLINIC USE     |
|--------------------|
| Clinic Ident.      |
| Date Vaccinated    |
| Manuf. and Lot No. |
| Site of injection  |

**FOR DATA PROCESSING USE ONLY (OPTIONAL)**

|   |   |   |   |   |   |  |  |
|---|---|---|---|---|---|--|--|
| VACCINE HISTORY: PLACE CHECK <input type="checkbox"/> |   | IN BOX IF HISTORY PREVIOUSLY SUBMITTED  |   |   |   |  |  |
| DTP:  | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | MEASLES: <u>    </u> / <u>    </u> / <u>    </u> | MUMPS: <u>    </u> / <u>    </u> / <u>    </u> |
| POLIO:  | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | RUBELLA: <u>    </u> / <u>    </u> / <u>    </u> |  |

## Measles

### VACCINE AVAILABILITY

The Immunization Program provides single-antigen measles vaccine for outbreak control, measles-rubella (MR), and measles mumps and rubella vaccine (MMR) for routine use.

Single-antigen measles vaccine will be provided only in an outbreak situation where the decision has been made to immunize children between 6 months and 12 months of age. This decision to vaccinate with single antigen measles vaccine must include consultation with the Montana Immunization Program. MMR vaccine is the vaccine of choice for routine immunization for measles. There is no contra-indication for reimmunization with the mumps or rubella component of the vaccine. Use of MR vaccine would depend on MMR availability.

See the attached ACIP statement and Important Information Form. Also refer to the Adult Immunization Recommendations on Measles and the Control of Communicable Diseases in Man.





Recommendations of the Immunization  
Practices Advisory Committee

**Measles Prevention**

*These revised recommendations of the Immunization Practices Advisory Committee (ACIP) on measles prevention update the previous recommendations (MMWR 1982;31:217-224,229-231) to include current information about vaccine effectiveness and measles elimination efforts. Although there are no basic changes in approach, the statement includes an additional option for outbreak control (revaccination of persons initially vaccinated at 12-14 months of age) and new recommendations for international travelers and medical personnel.*

**INTRODUCTION**

Measles (rubeola) is often a severe disease, frequently complicated by middle ear infection or bronchopneumonia. Encephalitis occurs in approximately one of every 2,000 reported cases; survivors often have permanent brain damage and mental retardation. Death, predominantly from respiratory and neurologic causes, occurs in one of every 3,000 reported measles cases. The risk of death is greater for infants and adults than for children and adolescents.

Subacute sclerosing panencephalitis (SSPE) is a "slow virus" infection of the central nervous system associated with measles virus. Widespread use of measles vaccine has led to the virtual disappearance of SSPE from the United States.

Contracting measles during pregnancy increases fetal risk. Most commonly, this risk involves premature labor and moderately increased rates of spontaneous abortion and of low birth weight. One study has suggested that measles infection in the first trimester may induce congenital malformations; confirmatory reports have not been published.

Before measles vaccine was available, more than 400,000 measles cases were reported each year in the United States. However, since virtually all children acquired measles, the true number of cases was probably more than 4 million per year (i.e., the entire birth cohort). Both the type of measles vaccine and the recommended age for measles vaccination have changed several times since 1963, when both an inactivated and a live, attenuated vaccine (Edmonston B strain) were licensed for use in the United States. The inactivated vaccine was used until 1967, and Edmonston B vaccine, until 1972. A live, further-attenuated Edmonston vaccine was first introduced in 1965 (Schwarz strain), and a similar vaccine (Moraten strain) was licensed in 1968. These further-attenuated vaccines cause fewer reactions than the Edmonston B vaccine yet are equally effective. The Moraten vaccine is the vaccine currently used in the United States.

Because of evidence of increased vaccine efficacy at older ages, the recommended age for vaccination, originally set at 9 months in 1963, was changed to 12 months in 1965 and to 15 months in 1976. Although vaccination is currently recommended at 15 months of age for optimal efficacy, vaccination as early as 12 months of age (on or after the first birthday) is considered appropriate evidence of measles immunity, and children vaccinated at 12-14 months of age are not routinely revaccinated. Vaccination as early as 6 months of age is recommended in settings of increased risk of disease.

**MEASLES ELIMINATION**

Since licensure of vaccine in 1963, the collaborative efforts of professional and voluntary medical and public health organizations in vaccination programs have resulted in a 98%-99% reduction in the reported incidence of measles in the United States. The number of reported measles cases decreased during the late 1960s and early 1970s to between 22,000 and 75,000 cases annually, with incidence rates falling dramatically in all age groups. Children <10 years old had the greatest decline in incidence, whereas older children had a slightly less dramatic decrease. As a result, the proportion of total cases occurring in different age groups changed so that by the period 1976-1980, 46% of cases occurred in children  $\geq 10$  years of age, compared with the period 1960-1964, when only 9.9% of cases occurred in this age group.

A Measles Elimination Program was announced in 1978, with a goal to eliminate indigenous measles from the United States by October 1, 1982. There are three components of this program: 1) achievement and maintenance of high levels of immunity, 2) effective surveillance of disease, and 3) aggressive outbreak control. As a result of these efforts, the number of cases of measles reported annually dropped from 26,871 in 1978 to approximately 13,500 in 1979 and 1980, to 3,124 in 1981. In 1982, the total fell to 1,714. In 1983, an all-time low of 1,497 reported cases was reached. However, the number of reported cases increased to 2,587 and 2,822, respectively, in 1984 and 1985. During 1986, a provisional total of 6,273 cases were reported.

Since 1984, a classification system has been used to differentiate cases that occurred because of failure to implement the current strategy (preventable cases) from cases that occurred despite appropriate strategy implementation (nonpreventable cases). Of the total cases provisionally reported in 1986, 36.4% were classified as preventable (Table 1). Preschool children 16 months-4 years of age were most likely to have preventable cases (83.2%), whereas only 29.4% of cases in school-aged children (5-19 years of age) were considered preventable. The greatest reason for nonpreventability was a history of previous measles vaccination on or after the first birthday (Table 2). These vaccine failures accounted for 59.8% of the nonpreventable cases and 38.0% of the total reported cases.

In the past several years, most of the outbreaks have occurred in school settings; in 1986, however, several large outbreaks involved communitywide transmission, primarily among unvaccinated preschool-aged children.

#### Impediments to Measles Elimination

Despite the great success achieved to date in reducing the occurrence of measles in the United States, the goal of eliminating indigenous measles has not yet been reached. Part of the problem is failure to implement the current strategy. Preventable cases (i.e., those in unvaccinated persons) account for approximately one-third of all cases. The age group with the largest proportion of preventable cases is the preschool group. Children at this age may not yet be enrolled in institutions covered by day-care or school-entry immunization requirements.

TABLE 1. Total and preventable measles cases, by age group — United States, 1986\*

| Age Group         | Total Cases    | Preventable  |               |
|-------------------|----------------|--------------|---------------|
|                   |                | No.          | (%)           |
| <16 months        | 1,229          | 0            | (0.0)         |
| 16 months-4 years | 1,225          | 1,019        | (83.2)        |
| 5-19 years        | 3,156          | 927          | (29.4)        |
| 20-29 years       | 460            | 332          | (72.2)        |
| ≥30 years         | 166            | 0            | (0.0)         |
| Unknown           | 19             | 0            | (0.0)         |
| <b>Total</b>      | <b>6,255 †</b> | <b>2,278</b> | <b>(36.4)</b> |

\*Provisional data.

†Cases with known preventability status.

TABLE 2. Measles cases, by preventability status — United States, 1986\*

| Classification                      | No.          | (%)                        |
|-------------------------------------|--------------|----------------------------|
| <b>Nonpreventable Cases</b>         |              |                            |
| Too young (<16 months)              | 1,230        | (19.7)                     |
| Too old (born before 1957)          | 194          | (3.1)                      |
| History of vaccination <sup>†</sup> | 2,377        | (38.0)                     |
| Importation by non-U.S. citizen     | 48           | (0.8)                      |
| Exemption <sup>‡</sup>              | 128          | (2.0)                      |
| Subtotal                            | 3,977        | (63.6)                     |
| <b>Preventable Cases</b>            | <b>2,278</b> | <b>(36.4)</b>              |
| <b>Total</b>                        | <b>6,255</b> | <b>(100.0)<sup>†</sup></b> |

\*Provisional data.

<sup>†</sup>Vaccinated on or after the first birthday.

<sup>‡</sup>Includes medical, religious, and philosophic exemptions.

<sup>§</sup>Cases with known preventability status.

A substantial proportion of cases occur among persons who have previously received vaccine. Theoretically, vaccine failures may be primary (the person never developed an adequate immune response to vaccination) or secondary (the person initially developed an adequate response but lost immunity over time). Some of the reported vaccine failures may be among persons whose records incorrectly indicate that they were properly vaccinated. Measles vaccine is at least 95% effective in children vaccinated at  $\geq 15$  months of age. However, efficacy may be slightly lower in persons vaccinated between 12 and 14 months of age, presumably because transplacental maternal antibody may persist beyond the first birthday in some children and interfere with effective immunization. There are no data to indicate that waning immunity of clinical importance is occurring after measles vaccination.

Another problem is importation of measles from outside the United States. Although importations account for a small proportion of cases (2%), they have initiated several outbreaks and, in some parts of the United States, may be responsible for more measles cases than the number indicated by available surveillance data.

#### **Augmentation of Measles Elimination Activities**

The Committee considered, in detail, current measles epidemiology and the measles elimination strategy, as well as potential modifications. It concluded that the current strategy needed more complete implementation to ensure that vaccination takes place at 15 months of age rather than being delayed, for example, until it is required for school entry.

After consideration of possible modifications of the measles elimination strategy, including administering two doses, lowering the age for vaccination, and routinely revaccinating those vaccinated between 12 and 14 months of age, the Committee determined that no change in the routine policy is indicated at present. Continued careful observation and analysis of measles epidemiology is indicated so that any necessary change in strategy can be implemented.

#### **MEASLES VIRUS VACCINE**

Live measles virus vaccine,\* available in the United States, is prepared in chick embryo cell culture. It is available in monovalent (measles only) form and in combinations: measles-rubella (MR) and measles-mumps-rubella (MMR) vaccines. All vaccines containing measles virus are recommended for use at 15 months of age under routine conditions. MMR is the vaccine of choice for routine vaccination programs. In all situations in which measles vaccine is to be used, a combination vaccine should be given if recipients are likely to be susceptible to rubella and/or mumps as well as to measles. There is no harm in revaccinating persons already immune to any of the components of MMR vaccine.

Measles vaccine produces a mild or inapparent noncommunicable infection. Measles antibodies develop in at least 95% of susceptible children vaccinated at  $\geq 15$  months of age. Both serologic and epidemiologic evidence extending through 23 years indicates that, although the titers of vaccine-induced antibody are lower than those following natural disease, the protection conferred appears to be durable.

#### **Vaccine Shipment and Storage**

Vaccine that has been improperly stored may not provide protection against measles. Although data indicate that current measles vaccine may be more thermostable than vaccine produced in the past, it should be kept at 2 C-8 C (35.6 F-46.4 F) or colder during storage. It must also be protected from light, which may inactivate the virus. Vaccine must be shipped at 10 C (50 F) or colder and may be shipped on dry ice.

#### **VACCINE USAGE**

##### **General Recommendations**

Persons are considered immune to measles only if they have documentation of 1) adequate immunization with live measles vaccine on or after the first birthday, 2) physician-diagnosed measles, or 3) laboratory evidence of measles immunity.

Most persons born before 1957 are likely to have been naturally infected and generally need not be considered susceptible. All other children, adolescents, and adults are considered susceptible and should be vaccinated if there are no contraindications (see **Precautions and Contraindications**). This includes persons who may be immune to measles but who lack adequate documentation of immunity. A parental report of immunization, by itself, is not considered adequate documentation. A physician should not provide an immunization record for a patient unless he/she has administered the vaccine or has seen a record documenting vaccination.

\*Official name: measles virus vaccine, live attenuated.

The most commonly used laboratory test for assessing immunity to measles has been the hemagglutination-inhibition (HI) test. Other sensitive assays, such as the enzyme immunoassay (EIA), are now being used by many laboratories. Probably most, if not all, persons with detectable antibody are immune. Routine serologic screening to determine measles immunity is not recommended.

#### **Dosage**

A single dose of live measles vaccine (as a monovalent or combination product) should be given subcutaneously in the volume specified by the manufacturer. There is no need for a "booster" dose of vaccine if vaccine is given on or after the first birthday.

#### **Age at Vaccination**

Measles vaccine is indicated for persons susceptible to measles, regardless of age, unless otherwise contraindicated (see below). Current evidence indicates that for a maximum seroconversion rate, measles vaccine should be given when children are  $\geq 15$  months of age. Because cases continue to occur in preschool children, increased emphasis must be placed on vaccinating children promptly at 15 months of age. It is particularly important to vaccinate young children  $\geq 15$  months of age before they might encounter measles in day-care centers or other environments where young children cluster.

The risk of complications from measles is high among infants  $< 1$  year of age. Therefore, considering the benefits and risks, the Committee recommends that infants as young as 6 months of age should be vaccinated with monovalent measles vaccine when exposure to natural measles is considered likely. Because infants vaccinated before the first birthday have a significantly lower rate of seroconversion, they should be revaccinated when they are 15 months old to ensure protection.

#### **Revaccination of Persons Vaccinated According to Earlier Recommendations**

**Previous vaccination with live vaccine:** Persons vaccinated with live measles vaccine before their first birthday should be identified and revaccinated. Some serologic studies show lower seroconversion and seroprevalence rates in children vaccinated between 12 and 14 months of age (80%-95%) than in those vaccinated at  $\geq 15$  months ( $> 95\%$ ). Many outbreak investigations have also found higher attack rates in persons vaccinated between 12 and 14 months of age than in those vaccinated at  $\geq 15$  months of age. However, a few other studies have not found a difference. Between 1965 and 1976, the recommended age for vaccination in the United States was 12 months; therefore, a large proportion of persons who are between 10 and 21 years of age in 1987 are likely to have been vaccinated when they were between 12 and 14 months of age. Because the vast majority of persons vaccinated between 12 and 14 months of age are fully protected against measles, routine revaccination of such persons is not warranted. However, if revaccination is requested, there is no immunologic or safety reason to deny the request. In an outbreak setting, such revaccination may be useful. (See **Outbreak Control.**)

Edmonston B vaccine was effectively administered with immune globulin (IG). However, the immune response to further-attenuated measles vaccine strains may be impeded by IG. Therefore, the Committee recommends that persons who received measles vaccine of unknown type or further-attenuated measles vaccine accompanied by IG should be revaccinated.

**Previous vaccination with killed vaccine or vaccine of unknown type:** Some persons who have received inactivated vaccine are at risk of contracting a severe atypical measles syndrome when exposed to the natural virus. Consequently, persons vaccinated at any age with inactivated vaccine (available in the United States from 1963 to 1967) and persons vaccinated with inactivated vaccine followed by live vaccine within 3 months should be revaccinated. Revaccination is particularly important when the risk of exposure to natural measles virus is increased, for example, during foreign travel.

A wide range (4%-55%) of prior recipients of killed measles vaccine who were revaccinated with live measles vaccine have reportedly had adverse reactions to the live vaccine. Most of these reactions have been mild, consisting of local swelling and erythema, with or without low-grade fever lasting 1-2 days. Rarely, more severe reactions, including prolonged high fevers and extensive local reactions requiring hospitalization, have been reported. However, prior recipients of killed measles vaccine are more likely to have serious illness when exposed to natural measles than when given live measles virus vaccine.

These same recommendations for revaccination apply to persons vaccinated between 1963 and 1967 with a vaccine of unknown type, since their only vaccination may have been with inactivated vaccine. Because killed measles vaccine was not distributed in the United States after 1967, persons

vaccinated after 1967 with a vaccine of unknown type need not be revaccinated if the original vaccination occurred on or after the first birthday and was not accompanied by IG.

#### **Individuals Exposed to Disease**

**Use of vaccine:** Exposure to measles is not a contraindication to vaccination. Available data suggest that live measles vaccine, if given within 72 hours of measles exposure, may provide protection and is preferable to the use of IG in persons at least 12 months of age if there is no contraindication. If the exposure does not result in infection, the vaccine should induce protection against subsequent measles infection.

**Use of IG:** IG can be given to prevent or modify measles in a susceptible person within 6 days after exposure. The recommended dose of IG is 0.25 ml/kg (0.11 ml/lb) of body weight (maximum dose = 15 ml). IG may be especially indicated for susceptible household contacts of measles patients, particularly contacts under 1 year of age, pregnant women, or immunocompromised persons, for whom the risk of complications is highest. The recommended dose of IG for immunocompromised persons is 0.5 ml/kg of body weight (maximum dose = 15 ml). If the individual is at least 15 months old and there is no contraindication to vaccination, live measles vaccine should be given 3 months later, by which time the passively acquired measles antibodies should have disappeared. IG should not be used to control measles outbreaks.

#### **SIDE EFFECTS AND ADVERSE REACTIONS**

Experience with more than 160 million doses of measles vaccine distributed in the United States through 1986 indicates an excellent record of safety. From 5% to 15% of vaccinees may develop a temperature of  $\geq 103$  F ( $\geq 39.4$  C) beginning about the fifth day after vaccination and usually lasting several days. Most persons with fever are otherwise asymptomatic. Transient rashes in approximately 5% of vaccinees have been reported. Central nervous system conditions including encephalitis and encephalopathy have been reported with a frequency of less than one case per million doses administered. The incidence rate of encephalitis or encephalopathy following measles vaccination is lower than the observed incidence rate of encephalitis of unknown etiology, suggesting that some or most of the reported severe neurologic disorders may be only temporally related to measles vaccination rather than due to vaccination. Limited data indicate that reactions to the vaccine are not age related.

#### **Personal and Family History of Convulsions**

As with the administration of any agent that may produce fever, some children may have a febrile seizure following measles vaccination. Although children with a personal or family history of seizures are at increased risk for developing idiopathic epilepsy, febrile seizures—including those following vaccinations—do not, in and of themselves, increase the probability of subsequent epilepsy or other neurologic disorders. Most convulsions following measles-containing vaccines are simple febrile seizures, and they occur in children without known risk factors. Recent data suggest that there is an increased risk of these convulsions among children with a prior history of convulsions or those with a history of convulsions in first-degree family members (i.e., siblings or parents). Although the precise risk cannot be determined, it appears to be low.

In developing vaccination recommendations concerning these children, the Committee considered a number of factors including risks from measles disease, the large number (5%-7%) of children with a personal or family history of convulsions, and the fact that convulsions following measles vaccine are uncommon and have not been associated with permanent brain damage. The Committee concluded that the benefits of immunizing children with a personal history of convulsions or a family history of convulsions in first-degree relatives greatly outweigh the risks. These children should be vaccinated in the same way that children without such histories are vaccinated.

Because the period for contracting vaccine-induced fever begins approximately 5 days after vaccination and lasts approximately 1 week, effective reduction of the risk of a febrile seizure is difficult. Prophylaxis with antipyretics is one alternative, but these agents probably would be ineffective if given after the onset of fever. To be effective, they would have to be given before the expected onset of fever and continued for another 5-7 days. Nevertheless, parents should closely observe children for fever during this period, and if fever occurs, the child should be treated appropriately.

Children who are receiving anticonvulsants should continue to take them after measles vaccination. Because protective levels of most currently available anticonvulsant drugs (e.g., phenobarbital) are not achieved for some time after the initiation of therapy, prophylactic use of these drugs does not seem feasible.

The parents of children who have either a personal or family history of seizures should be advised that such children have a small increased risk of seizures following vaccination. In particular, they should be told in advance of measles vaccination what to do in the unlikely event that the child has a seizure. The permanent medical record should document that the small risk of postvaccination seizures and the benefits of vaccination for these children have been discussed.

#### **Revaccination Risks**

There is no evidence of enhanced risk from receiving live measles vaccine to persons who are already immune to measles, either from vaccination or natural disease. (See Previous vaccination with killed vaccine or vaccine of unknown type.)

### **PRECAUTIONS AND CONTRAINDICATIONS**

#### **Pregnancy**

Live measles vaccine should not be given to women known to be pregnant or who are considering becoming pregnant within 3 months after vaccination. This precaution is based on the theoretical risk of fetal infection, which applies to the administration of any live virus vaccine to women who might be pregnant or who might become pregnant shortly after vaccination. No evidence exists to substantiate this theoretical risk from measles vaccine. Considering the importance of protecting adolescents and young adults against measles with its known serious risks, asking women if they are pregnant, excluding those who are, and explaining the theoretical risks to the others before vaccination are the recommended precautions in a measles immunization program.

#### **Febrile Illness**

Vaccine administration should not be postponed because of minor illnesses, such as mild upper-respiratory infections. However, vaccination of persons with severe febrile illnesses should generally be deferred until they have recovered. Considering the importance of measles protection, medical personnel should use every opportunity to vaccinate susceptible children.

#### **Allergies**

Hypersensitivity reactions following the administration of live measles vaccine are rare. Most of these reactions are minor and consist of wheal and flare or urticaria at the injection site. With more than 160 million doses of measles vaccine distributed in the United States, there have been at least five reported cases of immediate allergic reactions in children who had histories of anaphylactic reactions to egg ingestion. These reactions to vaccine could potentially have been life threatening. Four children experienced difficulty in breathing; one of these had hypotension. Persons with a history of anaphylactic reactions following egg ingestion (hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) should be vaccinated only with extreme caution. Protocols have been developed for vaccinating such persons (1). Evidence indicates that persons are not at increased risk if they have egg allergies that are not anaphylactic in nature. Such persons should be vaccinated in the usual manner. There is no evidence that persons with allergies to chickens or feathers are at increased risk of reaction to the vaccine.

Since measles vaccine contains trace amounts of neomycin (25µg), persons who have had anaphylactic reactions to topically or systemically administered neomycin should not receive measles vaccine. Most often, neomycin allergy is manifested as a contact dermatitis that is a delayed-type (cell-mediated) immune response rather than anaphylaxis. In such individuals the adverse reaction, if any, to 25µg of neomycin in the vaccine would be an erythematous, pruritic nodule or papule at 48-96 hours. A history of contact dermatitis to neomycin is not a contraindication to receiving measles vaccine. Live measles virus vaccine does not contain penicillin.

#### **Recent Administration of IG**

Vaccination should be deferred for 3 months after a person has received IG, whole blood, or other antibody-containing blood products because passively acquired antibodies might interfere with the response to the vaccine. If vaccine is given to a person who has received such products within the preceding 3 months, the person should be revaccinated. If IG is to be administered in preparation for international travel, administration of vaccine should precede IG by at least 2 weeks.

#### **Tuberculosis**

Tuberculosis may be exacerbated by natural measles infection. There is no evidence that the live measles virus vaccine has such an effect. Tuberculin skin testing is not a prerequisite for measles vaccination. If tuberculin testing is needed, it can be done the day of vaccination. Otherwise, it is prudent to wait 4-6 weeks after measles immunization before administering a tuberculin skin test, since measles vaccination may temporarily suppress tuberculin reactivity.

### **Altered Immunity**

Replication of the measles vaccine virus may be potentiated in patients with immune deficiency diseases and by the suppressed immune responses that occur with leukemia, lymphoma, generalized malignancy, acquired immunodeficiency syndrome (AIDS), or with certain therapies (corticosteroids, alkylating drugs, antimetabolites, or radiation). Patients with such conditions should not be given live measles virus vaccine. Since vaccinated persons do not transmit vaccine virus, the risk to these patients of being exposed to measles may be reduced by vaccinating their close susceptible contacts. Management of such persons, should they be exposed to measles, can be facilitated by prior knowledge of their immune status. If susceptible, they should receive IG following exposure (see below).

Patients with leukemia in remission whose chemotherapy has been terminated for at least 3 months may receive live virus vaccines. Persons infected with the human immunodeficiency virus (HIV) who are asymptomatic also can receive measles vaccine (2). Short-term corticosteroid therapy (<2 weeks), topical steroid therapy (e.g., nasal, skin), and intraarticular, bursal, or tendon injection with corticosteroids should not be immunosuppressive and do not contraindicate measles vaccine administration. However, measles vaccine should be avoided if systemic immunosuppressive levels are reached by prolonged, extensive, topical application.

### **Management of Patients with Contraindications to Measles Vaccine**

If immediate protection against measles is required for persons for whom measles vaccine is contraindicated, passive immunization with IG, 0.25 ml/kg (0.11 ml/lb) of body weight, should be given as soon as possible after known exposure (maximum dose = 15 ml). It is important to note, however, that IG in usual doses may not be effective in children with acute leukemia or other conditions associated with altered immunity. Consequently, for immunocompromised persons, the recommended dose of IG is 0.5 ml/kg of body weight (maximum dose = 15 ml).

### **SIMULTANEOUS ADMINISTRATION OF VACCINES**

Simultaneous administration of MMR, oral poliovirus vaccine (OPV), and diphtheria and tetanus toxoids and pertussis (DTP) vaccines results in seroconversion rates and rates of side effects similar to those observed when the vaccines are administered separately. On the basis of these results, the Committee recommends routine administration of MMR, OPV, and DTP simultaneously to susceptible persons at 15 months of age (3). Some health-care providers may prefer to continue administering MMR at 15 months of age, followed by DTP and OPV at 18 months of age, especially for patients who are known to be compliant with health-care recommendations.

### **ONGOING PROGRAMS**

The best means of reducing the incidence of measles is by having an immune population. Programs aimed at vaccinating children against measles at 15 months of age should be established and maintained in all communities. In addition, all other persons thought to be susceptible, regardless of age, should be vaccinated when they are identified, unless vaccine is otherwise contraindicated.

Official health agencies should take whatever steps are necessary, including development and enforcement of school immunization requirements, to achieve and maintain high immunization levels. Most states currently require evidence of immunity to measles for children enrolled in day-care centers. Enforcement of such requirements has been correlated with reduced measles incidence rates.

### **Vaccination for College Entry**

Measles outbreaks continue to be reported from settings where young adults are concentrated, such as colleges. Measles control in these places requires careful evaluation of susceptibility and vaccination of those who are susceptible. The Committee recommends that colleges and universities require proof of measles immunity as a condition for matriculation.

### **Vaccination for Medical Personnel**

Medical personnel are at higher risk for acquiring measles than the general population. Medical facilities should ensure that all employees born after 1956 have proof of immunity (See Vaccine Usage). Since a substantial proportion of medical personnel who have acquired measles were born before 1957, medical facilities may also consider requiring proof of measles immunity for older employees who may have occupational exposure to measles.

### **Outbreak Control**

All reports of suspected measles cases should be investigated rapidly. A measles outbreak exists in a community whenever one case of measles is confirmed. Once an outbreak occurs, preventing dissemination of measles depends on promptly vaccinating susceptible persons. Control activities should not be delayed until laboratory results on suspected cases are received. All persons who cannot

readily provide proof of immunity should be vaccinated or excluded from the setting (e.g., school). Documentation of vaccination should be considered adequate only if the date of vaccination is provided.

An effective means of terminating school outbreaks and quickly increasing rates of immunization is to exclude all children or adolescents from the outbreak area who cannot present valid evidence of immunity. Students can be readmitted immediately after vaccination. Experience with outbreak control indicates that almost all students who are excluded from the outbreak area because they lack evidence of immunity to measles quickly comply with requirements and can be readmitted to school. Pupils who have been exempted from measles vaccination because of medical, religious, or other reasons should be excluded until at least 2 weeks after the onset of rash in the last person with measles in the outbreak area.

Persons vaccinated between 12 and 14 months of age have been shown in some serologic and epidemic investigations to be at increased risk of acquiring measles compared with those vaccinated at  $\geq 15$  months of age. However, the increased risk of acquiring measles is small. Nevertheless, in many outbreaks, particularly in junior and senior high schools, persons vaccinated at 12-14 months of age appear to have played a substantial role in perpetuating transmission. Therefore, although the effectiveness of such a strategy in terminating outbreaks has not been demonstrated conclusively, the Committee recommends that revaccination of persons vaccinated at 12-14 months of age should be considered in outbreak settings, particularly in junior and senior high schools. If revaccination is recommended, local officials should establish a geographic zone of risk and limit revaccination to persons in this area. In the absence of an outbreak, routine revaccination of persons vaccinated at 12-14 months of age is not recommended.

#### **Importations**

Measles importations are a continuing source of reported measles cases in the United States. Although most importations result in limited transmission, several large outbreaks have occurred. If susceptible persons are exposed to a patient on a common carrier, such as an airplane, rapid reporting of such imported cases to state and local health departments is important. Other state health departments should be notified to identify exposed contacts as well as to initiate surveillance and control measures.

#### **SURVEILLANCE**

As the incidence rate of measles declines in the United States, aggressive surveillance becomes increasingly important. Known or suspected measles cases should be reported immediately to local health departments. Serologic confirmation should be attempted for every suspected case of measles that cannot be linked to a confirmed case. Reporting of suspected cases and implementation of outbreak-control activities should not be delayed while awaiting laboratory results. Effective surveillance of measles and its complications can delineate inadequate levels of protection, further define groups needing special attention, and assess the effectiveness of control activities.

Continuous and careful review of adverse events following measles vaccination is also important. All adverse events following vaccination should be evaluated and reported in detail to local and state health officials as well as to the vaccine manufacturer.

#### **Laboratory Diagnosis**

The traditional serologic diagnosis of measles requires a significant rise in antibody titer between the acute-phase and convalescent-phase serum specimen. However, a single specimen can be used to detect the presence of immunoglobulin M (IgM) antibody. Correct interpretation of serologic data depends on the proper timing of specimen collection in relation to onset of rash. This is especially important for interpreting negative IgM results, since IgM antibody peaks 10 days after rash onset and is usually undetectable 30 days after rash onset.

Asymptomatic reinfection with measles virus can occur in persons who have previously developed antibody, whether from vaccination or from natural disease. Symptomatic reinfections have been reported rarely. These infections have been accompanied by fourfold or greater rises in measles HI antibody titers, but measles-specific IgM antibodies have not been detected in appropriately timed serum specimens.

#### **INTERNATIONAL TRAVEL**

Persons traveling abroad should be immune to measles. Since the risk of serious complications and death is greater for adults than for children, it is especially important to protect young adults who have escaped measles and have not been vaccinated. Also, because measles vaccine is not 100% effective and because the risk of exposure to measles abroad may be substantially greater than in the United



States, consideration should be given to providing a one-time dose of measles vaccine to persons born after 1956 who travel abroad regardless of their previous vaccination status, unless there is a contraindication. Persons born before 1957 need not be considered susceptible. MMR is preferred for persons likely to be susceptible to mumps and rubella. If single-antigen measles vaccine is not readily available, travelers should receive MMR regardless of their immune status to mumps and rubella.

The age for measles vaccination should be lowered for children traveling to areas where measles is endemic or epidemic. Children 12-14 months of age should receive MMR vaccine before their departure (without need for revaccination). Children 6-11 months of age should receive a dose of single-antigen measles vaccine before departure and subsequently should receive MMR vaccine. Whereas the optimal age for revaccination is 15 months, the age for revaccination may be as low as 12 months if the child remains in a high-risk area. Since virtually all infants <6 months of age will be protected by maternally derived antibodies, no additional protection against measles in this age group is generally necessary.

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Recommendations of the Immunization  
Practices Advisory Committee

**Measles Prevention: Supplementary Statement**

**INTRODUCTION**

Since measles vaccine was introduced in the United States in 1963, the reported incidence of measles has decreased 99%, and indigenous measles transmission has been eliminated from most of the country. However, the goal to eliminate measles by October 1982 has not been met. Between 1981 and 1987, a low of 1497 (1983) to a high of 6282 (1986) cases were reported annually (1).

Two major types of outbreaks have occurred recently in the United States: those among unvaccinated preschool-aged children, including children younger than the recommended age for routine vaccination (i.e., 15 months), and those among vaccinated school-aged children (2). Large outbreaks among unvaccinated preschool-aged children have occurred in several inner-city areas. In these outbreaks, up to 88% of cases in vaccine-eligible children 16 months to 4 years of age were unvaccinated; as many as 40% of all cases occurred in children <16 months of age. Surveys of immunization levels in areas where these outbreaks occurred indicate that only 49%–65% of 2-year-olds had received measles vaccine (3).

Many outbreaks have occurred among school-aged children in schools with vaccination levels above 98%. These outbreaks have occurred in all parts of the country. Attack rates in individual schools have been low (1%–5%), and the calculated vaccine efficacy has been high. Primary vaccine failures (i.e., the approximately 2%–10% of vaccinees who fail to seroconvert after measles vaccination) have played a substantial role in transmission. In many of these outbreaks, children vaccinated at 12–14 months of age have had higher attack rates than those vaccinated at older ages (4).

In a few outbreaks (5,6), persons vaccinated in the more distant past, independent of age at vaccination, have been at increased risk for disease. However, no conclusive data indicate that waning vaccine-induced immunity itself has been a major problem.

**EVALUATION OF THE CURRENT MEASLES ELIMINATION STRATEGY**

The current measles elimination strategy calls for administration of one dose of measles vaccine at 15 months of age (7). A documented history of vaccination at or after 12 months of age, however, is considered appropriate vaccination. High immunization levels, along with careful surveillance and aggressive outbreak control, are the three essential elements of this strategy. The Immunization Practices Advisory Committee (ACIP) has periodically reviewed the current strategy and progress toward measles elimination (7). At a recent meeting, the ACIP again reviewed the epidemiology of measles in the United States as well as recommendations, made by a group of consultants convened by CDC in February 1988, for modification of the measles elimination strategy.

To increase vaccine coverage among preschool-aged children in inner-city areas, the ACIP considered it essential that research be conducted to determine ways to increase vaccine delivery. A variety of additions and/or changes in the current strategy were considered, including a routine two-dose measles vaccination schedule and a one-time mass revaccination for school-aged children. Two new strategies were recommended and are described below (Table 1).

**NEW RECOMMENDATIONS**

**Changes in vaccination schedule in areas with recurrent measles transmission among preschool-aged children**

To improve immunity levels in high-risk children <15 months of age, the ACIP recommends that a routine two-dose vaccination schedule for preschoolers be implemented in areas with recurrent measles transmission (i.e., counties with more than five reported cases among preschool-aged

children during each of the last 5 years). If recurrent measles transmission is occurring in defined parts of a county, local officials may elect to implement the routine two-dose schedule selectively in those parts. Health authorities in other urban areas that have experienced recent outbreaks among unvaccinated preschool-aged children may also consider implementing this policy. The first dose of measles vaccine should be administered at age 9 months or at the first health-care contact thereafter. Infants vaccinated before their first birthday should receive a second dose at or about 15 months of age. Single-antigen (monovalent) measles vaccine should be used for infants <1 year of age, and measles, mumps, and rubella vaccine (MMR), for persons vaccinated on or after the first birthday. Although some data suggest that children who do not respond to the first dose administered at a young age may have an altered immune response when revaccinated at an older age (8), there are no data to suggest that such children are not protected from measles (9).

If resource constraints do not permit a routine two-dose schedule, an acceptable alternative is to lower the age for routine vaccination to 12 months in those areas using one dose of MMR. If children also need diphtheria and tetanus toxoids and pertussis vaccine (DTP) and oral polio vaccine (OPV), these vaccines can be administered simultaneously with measles vaccine or MMR.

#### Changes in outbreak-control strategies for school-based outbreaks

Because of the prominent role that persons with primary vaccine failure are playing in measles transmission, the ACIP recommends the institution of some form of revaccination in outbreaks that occur in junior or senior high schools, colleges, universities, or other secondary institutions. In an outbreak, the ACIP recommends that, in affected schools as well as unaffected schools at risk of measles transmission from students in affected schools, all students and their siblings who received their most recent dose of measles vaccine before 1980 should be revaccinated. This date was selected for several reasons: 1) this strategy will capture almost all students vaccinated between 12 and 14 months of age, a group known to be at increased risk of primary vaccine failure, since the recommended age for routine vaccination was changed from 12 to 15 months in 1976; 2) it may be easier to identify students by year of vaccination than by age at vaccination; and 3) in some outbreak investigations, students vaccinated before 1978-1980 have been found to be at increased risk for measles. This is not felt to be due to waning immunity but rather to a higher rate of primary vaccine failure in persons vaccinated before that time. This higher rate may be due to different reasons, including less than optimal vaccine storage and handling or to the greater lability of the measles vaccine manufactured before a new stabilizer was used in 1979. While the exact date has not been determined, 1980 is a conservative cutoff. If all students vaccinated before 1980 cannot be revaccinated, then persons vaccinated before 15 months of age should be targeted.

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**TABLE 1. New recommendations for measles vaccination**

#### Areas with recurrent measles transmission\*

##### Two-dose schedule

|              |   |
|--------------|---|
| First dose:  | Monovalent measles vaccine at 9 months of age or first visit thereafter |
| Second dose: | MMR at 15 months of age   |

If a routine two-dose schedule is impractical, then MMR should be given routinely at 12 months of age.

##### Outbreaks in schools

Revaccinate all persons who received their most recent vaccination before 1980. If this is impractical, then children vaccinated before 15 months of age should be revaccinated.

\*County reporting more than five cases of measles among preschool-aged children during each of the previous 5 years.

# IMPORTANT INFORMATION ABOUT MEASLES, MUMPS, AND RUBELLA AND MEASLES, MUMPS, AND RUBELLA VACCINES

*Please Read This Carefully*

MMR 1/1/88

## WHAT IS MEASLES?

Measles is the most serious of the common childhood diseases. Usually it causes a rash, high fever, cough, runny nose, and watery eyes lasting 1 to 2 weeks. Sometimes it is more serious. It causes an ear infection or pneumonia in nearly 1 out of 10 children who get it. Approximately 1 child out of every 1,000 who get measles has an inflammation of the brain (encephalitis). This can lead to convulsions, deafness, or mental retardation. About 2 children in every 10,000 who get measles die from it. Measles can also cause a pregnant woman to have a miscarriage or give birth to a premature baby.

Before measles vaccine shots were available, there were hundreds of thousands of cases and hundreds of deaths each year. Nearly all children got measles by the time they were 15. Now, wide use of measles vaccine has nearly eliminated measles from the United States. However, if children are not vaccinated they have a high risk of getting measles, either now or later in life.

## WHAT IS MUMPS?

Mumps is a common disease of children. Usually it causes fever, headache, and inflammation of the salivary glands, which causes the cheeks to swell. Sometimes it is more serious. It causes a mild inflammation of the coverings of the brain and spinal cord (meningitis) in about 1 child in every 10 who get it. More rarely, it can cause inflammation of the brain (encephalitis) which usually goes away without leaving permanent damage. Mumps can also cause deafness. About 1 out of every 4 adolescent or adult men who get mumps develops painful inflammation and swelling of the testicles. While this condition usually goes away, on rare occasions it may cause sterility. Before mumps vaccine shots were available, there were more than 150,000 cases each year. Now, because of the wide use of mumps vaccine, the number of cases of mumps is much lower. However, if children are not vaccinated, they have a high risk of getting mumps.

## WHAT IS RUBELLA?

Rubella is also called German measles. It is a common disease of children and

may also affect adults. Usually it is very mild and causes a slight fever, rash, and swelling of glands in the neck. The sickness lasts about 3 days. Sometimes, especially in adult women, there may be swelling and aching of the joints for a week or two. Very rarely, rubella can cause inflammation of the brain (encephalitis) or cause a temporary bleeding disorder (purpura).

The most serious problem with rubella is that if a pregnant woman gets this disease, there is a good chance that she may have a miscarriage or that the baby will be born crippled, blind, or with other defects. The last big rubella epidemic in the United States was in 1964. Because of that epidemic, about 20,000 children were born with serious problems such as heart defects, deafness, blindness, or mental retardation because their mothers had rubella during the pregnancy.

Before rubella vaccine shots were available, rubella was so common that most children got the disease by the time they were 15. Now, because of the wide use of rubella vaccine, the number of cases of rubella is much lower. However, if children are not immunized, they have a high risk of getting rubella and possibly exposing a pregnant woman to the disease. If an unimmunized woman later becomes pregnant and catches rubella, she may have a defective baby. Since rubella is a mild illness, many women of childbearing age do not recall if they had rubella as a child. A simple blood test can show whether a person is immune to rubella or is not protected against the disease. Overall, about 1 in 5 women of childbearing age is not protected against rubella.

## MEASLES, MUMPS, AND RUBELLA VACCINES:

The vaccines are given by injection and are very effective. Ninety percent or more of people who get the shot will have protection, probably for life. Since protection is not as likely to occur if the vaccines are given very early in life, these vaccines should be given to children after their first birthday; measles-vaccine should be given at 15 months of age or older. Measles, mumps, and rubella vaccines can be given one at a time or in a combined vaccine

*(PLEASE READ OTHER SIDE)*

Forms provided by: Montana Immunization Program  
Dept. of Health & Environmental Sciences  
Helena, MT 59620

(measles-rubella [MR], measles-mumps-rubella [MMR] by a single shot. If they are given in combined vaccine, they should be given at 15 months of age or older.

Experts recommend that adolescents and adults—especially women of child-bearing age—who are not known to be immune to rubella should receive rubella vaccine (or MMR if they might also be susceptible to measles or mumps). Women should not receive the shot if they are pregnant or might become pregnant within 3 months. There is no known risk in being immunized against any or all three of these diseases if you are already immune to any of them.

#### POSSIBLE SIDE EFFECTS FROM THE VACCINES:

About 1 out of every 5 children will get a rash or slight fever lasting for a few days, 1 or 2 weeks after getting measles vaccine. Occasionally there is mild swelling of the salivary glands after mumps vaccination.

About 1 out of every 7 children who get rubella vaccine will get a rash or some swelling of the glands of the neck 1 or 2 weeks after the shot. About 1 out of every 20 children who get rubella vaccine will have some aching or swelling of the joints. This may happen anywhere from 1-3 weeks after the shot. It usually lasts only 2 or 3 days. Adults are more likely to have these problems with their joints—as many as 4 in 10 may have them. True arthritis with swelling of the joints is generally seen in less than two percent of adults receiving rubella vaccine. If pain or swelling of the joints occurs, it rarely lasts for more than a few days and rarely returns. Other temporary side effects, such as pain, numbness, or tingling in the hands and feet have also occurred but are very uncommon.

Although experts are not sure, it seems that very rarely children who get these vaccines may have a more serious reaction, such as inflammation of the brain (encephalitis), convulsions with fever, or nerve deafness.

With any vaccine or drug, there is a possibility that allergic or other more serious reactions or even death could occur.

#### PERSONAL OR FAMILY HISTORY OF CONVULSIONS:

Children who have had a convulsion and children who have a brother, sister, or parent who has ever had a convulsion are more likely to have a convulsion after receiving measles vaccine. Advisory committees of the United States Public Health Service and the American Academy of Pediatrics recommend that because of the overall risk of measles disease and the fact that the risk of

convulsions is still very low, children with a personal history of a convulsion and children with a family history of convulsions should receive measles vaccine. However, you should tell the person who is to give the immunization about such a history and discuss the possibility of using an anti-fever medicine.

#### WARNING—SOME PERSONS SHOULD NOT TAKE THESE VACCINES WITHOUT CHECKING WITH A DOCTOR:

- Anyone who is sick right now with something more serious than a cold.
- Anyone who had an allergic reaction to eating eggs so serious that it required medical treatment (does not apply to rubella vaccine).
- Anyone with cancer, leukemia, or lymphoma.
- Anyone with a disease that lowers the body's resistance to infection.
- Anyone taking a drug that lowers the body's resistance to infection (such as cortisone, prednisone or certain anticancer drugs).
- Anyone who has received gamma globulin (immune globulin) within the preceding 3 months.
- Anyone who had an allergic reaction to an antibiotic called neomycin so serious that it required medical treatment.

#### PREGNANCY:

Measles, mumps, and rubella vaccines are not known to cause special problems for pregnant women or their unborn babies. However, doctors usually avoid giving any drugs or vaccines to pregnant women unless there is a specific need. To be safe, pregnant women should not get these vaccines. A woman who gets any of these vaccines should wait 3 months before getting pregnant.

Immunizing a child whose mother is pregnant is not dangerous to the pregnancy.

#### QUESTIONS:

If you have any questions about measles, mumps, or rubella immunization, please ask us now or call your doctor or health department before you sign this form.

#### REACTIONS:

If the person who received the vaccine has a convulsion or other serious reaction the person should be seen promptly by a doctor.

If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after immunization, please report it to:

### PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

I have read or have had explained to me the information on this form about measles, mumps, and rubella and measles, mumps, and rubella vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of measles, mumps, and rubella vaccine and request that the vaccine checked below be given to me or to the person named below for whom I am authorized to make this request.

Vaccine to be given:  Measles  Mumps  
 Rubella  Measles-Rubella  Measles-Mumps-Rubella

MMR 1/1/88

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                            |            |       |           |      |
|---|------------|-------|-----------|------|
| Last Name   | First Name | MI    | Birthdate | Age  |
| Address   |            |       |           |      |
| City  | County     | State | Zip       |      |
| X<br>Signature of person to receive vaccine or person authorized to make the request. |            |       |           | Date |

| FOR CLINIC USE     |
|--------------------|
| Clinic Ident.      |
| Date Vaccinated    |
| Manuf. and Lot No. |
| Site of Injection  |

| FOR DATA PROCESSING USE ONLY (OPTIONAL) |             |        |        |        |  |          |        |                |        |
|---|-------------|--------|--------|--------|--|----------|--------|----------------|--------|
| VACCINE HISTORY                         | PLACE CHECK |        |        |        | IN BOX IF HISTORY PREVIOUSLY SUBMITTED |          |        |                |        |
| DTP:                                    | m/d/yr      | m/d/yr | m/d/yr | m/d/yr | m/d/yr                                 | MEASLES: | m/d/yr | MUMPS:         | m/d/yr |
| POLIO:                                  | m/d/yr      | m/d/yr | m/d/yr | m/d/yr | m/d/yr                                 | RUBELLA: | m/d/yr | HAEMOPHILUS b: | m/d/yr |

Rubella

VACCINE AVAILABILITY

Single antigen rubella vaccine is available -- but not supplied by the Immunization Program. Measles and rubella vaccine (MR) combined are provided for adult susceptibles. MMR vaccine is the vaccine of choice for routine immunization for measles. There is no contraindication for reimmunization with the mumps or measles component of the vaccine. Use of MR vaccine would depend on MMR availability.

See ACIP statement and Important Information Form. Also, refer to the Adult Immunization Recommendation on rubella and the Control of Communicable Diseases in Man.





Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**Rubella Prevention**

*These revised Immunization Practices Advisory Committee (ACIP) recommendations for the prevention of rubella update the previous recommendations (MMWR 1981;30:37-42, 47) to include current information about vaccine effectiveness, duration of immunity, vaccination in pregnancy, and progress in controlling congenital rubella syndrome.*

*While there are no basic changes in approach, the available epidemiologic data indicate that the elimination of congenital rubella syndrome can be achieved and even hastened by focusing particular attention on more effective delivery of vaccine to older individuals—particularly women of childbearing age. The importance of vaccinating preschool-aged children is also emphasized. As the incidence of rubella declines, serologic confirmation of cases becomes more important. Recommendations for international travel are included.*

**INTRODUCTION**

Rubella is a common childhood rash disease. It is often overlooked or misdiagnosed because its signs and symptoms vary. The most common—postauricular and suboccipital lymphadenopathy, arthralgia, transient erythematous rash, and low fever—may not be recognized as rubella. Similar exanthematous illnesses are caused by adenoviruses, enteroviruses, and other common respiratory viruses. Moreover, 25%-50% of infections are subclinical. Transient polyarthralgia and polyarthritis sometimes accompany or follow rubella. Among adults, and particularly among women, joint manifestations occur so frequently (up to 70%), they may be considered an expected manifestation of adult infection. Central nervous system complications and thrombocytopenia have been reported at rates of 1/6,000 cases and 1/3,000 cases, respectively. The former is more likely to occur among adults; the latter, among children.

By far the most important consequences of rubella are the abortions, miscarriages, stillbirths, and fetal anomalies that result from rubella infection in early pregnancy, especially in the first trimester. Preventing fetal infection and consequent congenital rubella syndrome (CRS) is the objective of rubella immunization programs.

The most commonly described anomalies associated with CRS are ophthalmologic (cataracts, microphthalmia, glaucoma, chorioretinitis), cardiac (patent ductus arteriosus, pulmonary artery stenosis, atrial or ventricular septal defects), auditory (sensorineural deafness), and neurologic (microcephaly, meningoencephalitis, mental retardation). In addition, infants with CRS frequently are retarded in growth and have radiolucent bone disease, hepatosplenomegaly, thrombocytopenia, and purpuric skin lesions (blueberry-muffin appearance). Moderate and severe cases of CRS are readily recognizable at birth; mild cases (e.g., those with only slight cardiac involvement or deafness) may not be detected for months or even years after birth. Although CRS has been estimated to occur among 20%-25% or more of infants born to women who acquire rubella during the first trimester, the actual risk of infection and subsequent defects may be considerably higher. If infected infants are followed for at least 2 years, up to 80% of infants will be found to be affected. The risk of any defect falls to approximately 10%-20% by the 16th week, with defects rarely occurring after infection beyond the 20th week. However, fetal infection without clinical stigmata of CRS can occur at any stage of pregnancy. Inapparent maternal rubella infection can also result in malformations.

The average life-time expenditure associated with a CRS infant has recently been estimated to be in excess of \$220,000, which includes costs associated with institutionalization of the retarded, blind, and/or deaf and the education of hearing- and sight-impaired teenagers and adolescents.

Postinfection immunity appears to be long-lasting. However, as with other viral diseases, reexposure to natural rubella occasionally leads to reinfection without clinical illness or detectable viremia. Because many rash illnesses may mimic rubella infection, and because many rubella infections are unrecognized, the only reliable evidence of immunity to rubella is the presence of specific antibody. Laboratories that regularly perform antibody testing are generally the most reliable, because their reagents and procedures are strictly standardized (see below).

Before rubella vaccines became available in 1969, most rubella cases occurred among school-aged children. Since control of rubella in the United States was based on interrupting transmission, the primary target group for

vaccine was children of both sexes. Secondary emphasis was placed on vaccinating susceptible adolescents and young adults, especially women. By 1977, vaccination of children 12 months of age and older had resulted in a marked decline in the reported rubella incidence among children and had interrupted the characteristic 6- to 9-year rubella epidemic cycle. However, this vaccination strategy had less effect on reported rubella incidence among persons 15 years of age and older (i.e., childbearing ages for women) who subsequently accounted for more than 70% of reported rubella patients with known ages. Approximately 10%-20% of this latter population continued to be susceptible, a proportion similar to that of prevaccine years, and reported CRS continued at a low but constant endemic level (an annual average of 32 reported confirmed and compatible cases\* between 1971 and 1977).

Increased efforts were made to effectively vaccinate junior and senior high school students and to enforce rubella immunization requirements for school entry. All susceptible military recruits began to receive rubella vaccine. Published accounts of rubella outbreaks in hospitals caused concern about the need to screen and/or vaccinate susceptible personnel. A number of states stressed the need for ensuring proof of rubella immunity (i.e., documentation of vaccination or seropositivity) for college entrance. These factors, combined with the 1977 Childhood Immunization Initiative and the 1978 Measles Elimination effort (which encouraged use of combined vaccines containing measles and rubella antigens), have led to decreases in reported rubella in all age groups.

The number of rubella vaccine doses administered in the public sector to persons 15 years of age and older doubled between 1978 and 1981. By 1980, reported incidence among adolescents and young adults was lower than that among young children. Children under 5 years of age had the highest overall incidence and accounted for approximately one-fourth of all rubella patients with known ages. Compared with prevaccine years, by 1981 the overall reported rate of rubella had declined by 96%, with a 90% or greater decrease in cases in all age groups. Predictably, the number of reported confirmed and compatible CRS cases started to decline further (provisional totals of 14 cases for 1980 and 10 for 1981).

By 1982, more than 118 million doses of rubella virus vaccine had been distributed in the United States. However, the reported incidence of rubella rose slightly between 1981 and 1982 due to isolated outbreaks in adolescent and young adult populations and particularly in hospitals and universities. As expected, the reported number of confirmed and compatible CRS cases had increased slightly (a provisional total of 11 for 1982). While children under 5 years of age still had the highest reported incidence of rubella, they accounted for only half as many cases in 1982 as in 1981 (20% compared with 38%). In contrast, persons 15 years of age or older accounted for almost twice as many cases in 1982 as in 1981 (62% compared with 36%) and had a twofold increase in their estimated rate (from 0.4 cases/100,000 population in 1981 to 0.8/100,000 in 1982). The greatest increase in reported rates within this age group occurred in those 25-29 years of age.

The provisional data for 1983 indicate a record low number of rubella cases (934) was reported to CDC; the reported confirmed and compatible CRS total is only four. However, assuming the slight increase in reported rubella among older individuals between 1981 and 1982 was real, it indicates that rubella in postpubertal populations is still a problem in this country and continues to deserve particular attention.

#### **RUBELLA SEROLOGY TESTING AND IMMUNITY**

Until recently, hemagglutination-inhibition (HI) antibody testing has been the most frequently used method of screening for the presence of rubella antibodies. However, the HI test is now being supplanted by a number of equally or more sensitive assays to determine rubella immunity. These include latex agglutination, fluorescence immunoassay, passive hemagglutination, hemolysis-in-gel, and enzyme immunoassay (EIA) tests. When adults who have failed to produce detectable HI antibodies following vaccination have been examined more closely, almost all have had detectable antibody by a more sensitive test. Similarly, a small number of children who initially seroconverted has lost detectable HI antibody over 10 years of follow-up. However, almost all have had detectable antibody by more sensitive tests. Immunity was confirmed in a number of these children by documenting a booster response (i.e., no immunoglobulin M [IgM] antibody and a rapid rise and fall in immunoglobulin G [IgG] antibody) following revaccination.

Although it is recognized that some individuals possess antibody levels following previous vaccination or infection that are below the detectable level of the reference HI test, the clinical significance of such low level antibody has not been well documented outside the study setting. Limited data suggest that, on rare occasions, viremia has occurred in persons with low antibody levels. Further study is warranted to assess the appropriate interpretation of antibodies detectable only by these more sensitive tests. Use of an internationally accepted standard

\*A confirmed case has at least one defect in categories A or B and laboratory confirmation of rubella infection. A compatible case has any two complications listed in A or one from A and one from B without laboratory confirmation.

- A. Cataracts/congenital glaucoma (either or both count as one); congenital heart disease, loss of hearing, pigmentary retinopathy.
- B. Purpura, splenomegaly, jaundice, microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease.

would greatly facilitate resolution of this uncertainty. The available data continue to support the fact that any level of detectable antibody should be considered presumptive evidence of immunity.

#### **LIVE RUBELLA VIRUS VACCINE**

The live rubella virus vaccine<sup>†</sup> currently distributed in the United States is prepared in human diploid cell culture. In January 1979, this vaccine (RA 27/3) replaced the HPV-77:DE-5 vaccine grown in duck embryo cell culture. Although both subcutaneous and intranasal administration of the vaccine have been studied, it is licensed only for subcutaneous administration. The vaccine is produced in monovalent form (rubella only) and in combinations: measles-rubella (MR), rubella-mumps, and measles-mumps-rubella (MMR) vaccines.

In clinical trials, 95% or more of susceptible persons who received a single dose of rubella vaccine when they were 12 months of age or older developed antibody. Clinical efficacy and challenge studies have shown that more than 90% of vaccinees can be expected to have protection against both clinical rubella and asymptomatic viremia for a period of at least 15 years. Based on available follow-up studies, vaccine-induced protection is expected to be lifelong. Therefore, a history of vaccination is presumptive evidence of immunity.

Although vaccine-induced titers are generally lower than those stimulated by rubella infection, vaccine-induced immunity usually protects against both clinical illness and viremia after natural exposure. There have been, however, a small number of reports indicating that viremic reinfection following exposure may occur in vaccinated individuals with low levels of detectable antibody. The frequency and consequences of this phenomenon are currently unknown, but its occurrence is believed rare. Such reports are to be expected, since there are also rare reports of clinical reinfection and fetal infection following natural immunity.

Some vaccinees intermittently shed small amounts of virus from the pharynx 7-28 days after vaccination. However, studies of more than 1,200 susceptible household contacts and experience gained over 15 years of vaccine use have yielded good evidence that vaccine virus is not transmitted. These data indicate that vaccinating susceptible children, whose mothers or other household contacts are pregnant, does not present a risk. Rather, vaccination of such children provides protection for these pregnant women.

#### **Vaccine Shipment and Storage**

Administering improperly stored vaccine may result in lack of protection against rubella. During storage, before reconstitution, rubella vaccine must be kept at 2 C-8 C (35.6 F-46.4 F) or colder. It must also be protected from light, which may inactivate the virus. Reconstituted vaccine should be discarded if not used within 8 hours. Vaccine must be shipped at 10 C (50 F) or colder and may be shipped on dry ice.

#### **VACCINE USE**

##### **General Recommendations**

Persons 12 months of age or older should be vaccinated, unless they are immune. Persons can be considered immune to rubella only if they have documentation of:

1. Laboratory evidence of rubella immunity or
2. Adequate immunization with rubella vaccine on or after the first birthday.

The clinical diagnosis of rubella is unreliable and should not be considered in assessing immune status.

All other children, adolescents, and adults—particularly women—are considered susceptible and should be vaccinated if there are no contraindications (see below). This includes persons who may be immune to rubella but who lack adequate documentation of immunity. Vaccinating children protects them against rubella and prevents their spreading the virus. Vaccinating susceptible postpubertal females confers individual protection against rubella-induced fetal injury. Vaccinating adolescent or adult females and males in high-risk population groups, such as those in colleges, places of employment, or military bases, protects them against rubella and reduces the chance of epidemics. This is exemplified by the experience with vaccinating all military recruits, which has virtually eliminated rubella from military bases. Similar results could be achieved by ensuring proof of immunity of all employees, all college students and staff, and all hospital personnel, including physicians, nurses, health-profession students, technicians, dietary workers, etc.

As discussed above, it is generally believed that any detectable antibody titer specific for rubella (whether resulting from vaccination or from naturally acquired rubella), even if very low, should be considered evidence of protection against subsequent viremic infection—including the reported "reinfection" of persons with low levels of antibody demonstrated by boosts in antibody titer. This suggests that immune females reinfected during pregnancy would be unlikely to infect their fetuses. Moreover, because there is very little pharyngeal excretion, there appears to be no risk to susceptible contacts in such reinfection settings. In view of the data on reinfection accumulated during the past decade, the ACIP sees no reason to revaccinate persons with low levels of rubella antibody. Rather, more attention should be directed toward vaccinating the truly susceptible population.

<sup>†</sup>Official name: Rubella Virus Vaccine, Live.

## **Dosage**

A single dose of 0.5 cc of reconstituted vaccine (as a monovalent or preferably a combination product such as MR or MMR) should be administered subcutaneously.

## **Age at Vaccination**

Live rubella virus is recommended for all children 12 months of age or older. It should not be given to younger infants, because persisting maternal antibodies may interfere with seroconversion. When the rubella vaccine is part of a combination that includes the measles antigen, the combination vaccine should be given to children at 15 months of age or older to maximize measles seroconversion. Older children who have not received rubella vaccine should be vaccinated promptly. Because a history of rubella illness is not a reliable indicator of immunity, all children should be vaccinated unless there are contraindications (see below).

## **Vaccination of Women of Childbearing Age**

The ACIP has weighed several factors in developing recommendations for vaccinating women of childbearing age against rubella. Although there may be theoretical risks in giving rubella vaccine during pregnancy, available data on previously and currently available rubella vaccines indicate that the risk, if any, of teratogenicity from live rubella vaccines is quite small. As of December 31, 1983, CDC has followed to term 214 known rubella-susceptible pregnant females who had been vaccinated with live rubella vaccine within 3 months before or 3 months after conception. Ninety-four received HPV-77 or Cendehill vaccines, one received vaccine of unknown strain, and 119 received RA 27/3 vaccine. None of the 216 babies (two of the mothers receiving RA 27/3 vaccine delivered twins) has malformations compatible with congenital rubella infection. This finding includes the four infants born to these susceptible women who had serologic evidence of subclinical infection. (Three of the infants were exposed to HPV-77 or Cendehill vaccine; one was exposed to RA 27/3 vaccine.)

Based on the experience to date, the maximum estimated theoretical risk of serious malformations attributable to RA 27/3 rubella vaccine, derived from the binomial distribution, is 3%. (If the 95 susceptible infants exposed to other rubella vaccines are included, the maximum theoretical risk is 1.7%.) However, the observed risk with both the HPV-77 or Cendehill and RA 27/3 strains of vaccine is zero. In either case, this risk is far less than the 20% or greater risk of CRS associated with maternal infection during the first trimester of pregnancy.

Although experience with the RA 27/3 vaccine is more limited than that with the other rubella vaccines, rubella vaccine virus has been isolated from abortion material from one (3%) of 32 susceptible females who had been given RA 27/3 vaccine while pregnant, whereas virus was isolated from abortion material from 17 (20%) of 85 susceptible females who had been given HPV-77 or Cendehill vaccines while pregnant. This provides additional evidence that the RA 27/3 vaccine does not pose any greater risk of teratogenicity than did the HPV-77 or Cendehill vaccines.

Therefore, the ACIP believes that the risk of vaccine-associated defects is so small as to be negligible and should not ordinarily be a reason to consider interruption of pregnancy. However, a final decision about interruption of pregnancy must rest with the individual patient and her physician.

The continuing occurrence of rubella among women of childbearing age and the lack of evidence for teratogenicity from the vaccine indicate strongly that increased emphasis should continue to be placed on vaccinating susceptible adolescent and adult females of childbearing age. However, because of the theoretical risk to the fetus, females of childbearing age should receive vaccine only if they say they are not pregnant and are counseled not to become pregnant for 3 months after vaccination. In view of the importance of protecting this age group against rubella, reasonable practices in a rubella immunization program include: (1) asking females if they are pregnant, (2) excluding those who say they are, and (3) explaining the theoretical risks to the others.

## **Use of Vaccine Following Exposure**

There is no conclusive evidence that giving live rubella virus vaccine after exposure will prevent illness. Additionally, there is no evidence that vaccinating an individual incubating rubella is harmful. Consequently, since a single exposure may not cause infection and postexposure vaccination will protect an individual exposed in the future, vaccination is recommended, unless otherwise contraindicated.

## **Use of Human Immune Globulin Following Exposure**

Immunoglobulin (IG) given after exposure to rubella will not prevent infection or viremia, but it may modify or suppress symptoms and create an unwarranted sense of security. The routine use of IG for postexposure prophylaxis of rubella in early pregnancy is not recommended. Infants with congenital rubella have been born to women given IG shortly after exposure. IG might be useful only when a pregnant woman who has been exposed to rubella would not consider termination of pregnancy under any circumstances.

## **Recent Administration of IG**

Vaccine should be administered about 2 weeks before or deferred for about 3 months after receipt of IG, because passively acquired antibodies might interfere with the response to the vaccine. On the other hand, previous administration of anti-Rho (D) immune globulin (human) or blood products does not generally interfere with an

immune response and is not a contraindication to postpartum vaccination. However, in this situation, 6- to 8-week postvaccination serologic testing should be done on those who have received the globulin or blood products to assure that seroconversion has occurred. Obtaining laboratory evidence of seroconversion in other vaccinees is not necessary.

#### **SIDE EFFECTS AND ADVERSE REACTIONS**

Children sometimes have vaccine side effects, such as low-grade fever, rash and lymphadenopathy. Up to 40% of vaccinees in large-scale field trials have had joint pain, usually of the small peripheral joints, but frank arthritis has generally been reported for fewer than 2%. Arthralgia and transient arthritis occur more frequently and tend to be more severe in susceptible women than in children. While up to 3% of susceptible children have been reported to have arthralgia, arthritis has rarely been reported in these vaccinees. By contrast, up to 10%-15% of susceptible female vaccinees have been reported to have arthritis-like signs and symptoms. Transient peripheral neuritic complaints, such as paresthesias and pain in the arms and legs, have also very rarely occurred.

When joint symptoms or nonjoint-associated pain and paresthesias do occur, they generally begin 3-25 days (mean 8-14 days) after immunization, persist for 1-11 days (mean 2-4 days) and rarely recur. Adults with joint problems usually have not had to disrupt work activities. The occasional reports of persistent or recurrent joint signs and symptoms probably represent a rare phenomenon. No joint destruction has been reported. While the presence of immune complexes following vaccination has been reported to be associated with arthralgia and arthritis, the available data are still inconclusive. Comparable studies on naturally infected persons have not been conducted. Likewise, there is no clear association between joint symptoms and persistence of rubella virus in lymphocytes.

The vast majority of published data indicate that only susceptible vaccinees have side effects of vaccination. There is no conclusive evidence of an increased risk of these reactions for persons who are already immune when vaccinated.

Although vaccine is safe and effective for all persons 12 months of age or older, its safety for the developing fetus is not fully known. Therefore, though the risk, if any, appears to be minimal, rubella vaccine should not be given to women known to be pregnant because of the theoretical risk of fetal abnormality caused by vaccine virus (see above).

#### **PRECAUTIONS AND CONTRAINDICATIONS**

##### **Pregnancy**

Pregnant women should not be given rubella vaccine. If a pregnant woman is vaccinated or if she becomes pregnant within 3 months of vaccination, she should be counseled on the theoretical risks to the fetus. As noted above, rubella vaccination during pregnancy should not ordinarily be a reason to consider interruption of pregnancy. Instances of vaccination during pregnancy should be reported through state health departments to the Division of Immunization, Center for Prevention Services, CDC.

Because of the increasing number of cases reported to CDC, the experience with known susceptibles is becoming well defined. Therefore, CDC now encourages reporting only cases involving women known to be susceptible at the time of vaccination.

##### **Febrile Illness**

Vaccination of persons with severe febrile illness should be postponed until recovery. However, susceptible children with mild illnesses, such as upper respiratory infection, should be vaccinated. Considering the importance of protecting against rubella, medical personnel should use every opportunity to vaccinate susceptible individuals.

##### **Allergies**

Hypersensitivity reactions very rarely follow the administration of live rubella vaccine. Most of these reactions are considered minor and consist of wheal and flare or urticaria at the injection site.

Live rubella vaccine is produced in human diploid cell culture. Consequently, a history of anaphylactic reactions to egg ingestion needs to be taken into consideration only if measles or mumps antigens are to be included with rubella vaccine.

Since rubella vaccine contains trace amounts of neomycin (25 µg), persons who have experienced anaphylactic reactions to topically or systematically administered neomycin should not receive rubella vaccine. Most often, neomycin allergy is manifested as a contact dermatitis, which is a delayed-type (cell-mediated) immune response, rather than anaphylaxis. In such individuals, the adverse reaction, if any, to 25 µg of neomycin in the vaccine would be an erythematous, pruritic nodule or papule at 48-96 hours. A history of contact dermatitis to neomycin is not a contraindication to receiving rubella vaccine. Live rubella vaccine does not contain penicillin.

### Altered Immunity

Replication of live rubella vaccine virus may be potentiated in patients with immune deficiency diseases and by the suppressed immune responses that occur with leukemia, lymphoma, generalized malignancy, and therapy with corticosteroids, alkylating drugs, antimetabolites, and radiation. Patients with such conditions should not be given live rubella virus vaccine. Since vaccinated persons do not transmit vaccine virus, the risk to these patients of being exposed to rubella may be reduced by vaccinating their close susceptible contacts. Management of such patients, should they be exposed to rubella, can be facilitated by prior knowledge of their immune status.

Patients with leukemia in remission whose chemotherapy has been terminated for at least 3 months may receive live virus vaccines for infections to which they are still susceptible (i.e., have neither had the disease nor the vaccine before developing leukemia). The exact interval after discontinuing immunosuppression that coincides with the ability to respond to individual vaccines is not known. Experts vary in their judgments from 3 months to 1 year.

Short-term (less than 2 weeks) corticosteroid therapy, topical steroid therapy (e.g., nasal, skin), and intra-articular, bursal, or tendon injection with corticosteroids should not be immunosuppressive and do not necessarily contraindicate live virus vaccine administration. However, live vaccines should be avoided if systemic immunosuppressive levels are reached by topical application.

### Simultaneous Administration of Certain Live Virus Vaccines

See "General Recommendations on Immunization," (*MMWR* 1983;32:2-8,13-17).

### ELIMINATION OF CRS

Widespread vaccination of school-aged children since 1969 has effectively prevented major epidemics of rubella and congenital rubella in this country. With continued vaccination of children at levels approaching 100%, an immune birth cohort will eventually replace the 10%-15% of persons of childbearing age currently susceptible to rubella, and rubella can be expected to disappear. Since this process will take 10-30 years, cases of CRS can still be expected to occur.

Elimination of CRS can be hastened by intensifying and expanding existing efforts to vaccinate susceptible adolescents and young adults, particularly young women of childbearing age, along with continuing routine vaccination of children. Effective vaccination of all susceptible children in junior and senior high schools can be expected to contribute greatly to the elimination of CRS. Over the last 3 years, such efforts have resulted in decreases in the reported incidence of rubella in all persons and in the incidence of reported CRS. In 1982, the rubella cases that occurred were largely in older, post-school-aged populations, clearly indicating that rubella in postpubertal populations is still a problem in this country.

The major components of a strategy to eliminate CRS are achieving and maintaining high immunization levels, accurate surveillance of rubella and CRS, and prompt outbreak-control measures. The following recommendations are presented to help preserve the level of rubella and CRS control already achieved and to bring about the further reduction in susceptibility that will be required to achieve elimination of CRS.

#### Ongoing Programs

The primary strategy for eliminating CRS in the United States is to interrupt rubella transmission by achieving and maintaining high immunization levels in all children. Official health agencies should take steps, including developing and enforcing immunization requirements, to assure that all students in grades kindergarten through 12 are protected against rubella, unless vaccination is contraindicated. School entry laws should be vigorously enforced. States that do not require proof of immunity of students at all grade levels should consider expanding existing laws or regulations to include the age groups not yet protected.

Recent age-specific data indicate that preschool-aged children account for an important proportion of reported rubella cases. Proof of rubella immunity for attendance at day-care centers should be required and enforced. Licensure should depend on such requirements.

To hasten the elimination of CRS, new emphasis will have to be directed towards vaccinating susceptible females of childbearing age—the group at highest risk. A multifaceted approach is necessary. A number of approaches are discussed below.

#### Premarital Screening and Vaccination

Routine premarital testing for rubella antibody identifies many susceptible women before pregnancy. Documented histories of rubella vaccination or serologic evidence of immunity should be considered acceptable proof of immunity. To ensure a significant reduction in susceptibles through premarital screening, more aggressive follow-up of women found to be susceptible will be required.

#### Postpartum Vaccination

Prenatal screening should be carried out on all pregnant women not known to be immune. Women who have just delivered babies should be vaccinated before discharge from the hospital, unless they are known to be

immune. Although such women are unlikely to become pregnant, counseling to avoid conception for 3 months following vaccination is still necessary. It is estimated that postpartum vaccination of all women not known to be immune could prevent one-third to one-half of current CRS cases. Breast-feeding is not a contraindication to vaccination, even though virus may be excreted in breast milk, and infants may be infected. Vaccination should be extended to include all postabortion settings.

#### **Routine Vaccination in any Medical Setting**

Vaccination of susceptible women of childbearing age should be part of routine general medical and gynecologic outpatient care, should take place in all family-planning settings, and should become routine before discharge from a hospital for any reason, if there are no contraindications (see above). Vaccine should be offered to adults, especially women of childbearing age, anytime contact is made with the health-care system, including when children are undergoing routine examinations or immunizations.

#### **Vaccination of Medical Personnel**

Medical personnel, both male and female (volunteers, trainees, nurses, physicians, etc.), who might transmit rubella to pregnant patients or other personnel, should be immune to rubella. Consideration should be given to making rubella immunity a condition for employment.

#### **Vaccination of Workers**

Ascertainment of rubella immune status and availability of rubella immunization should be components of the health-care program in places where women of childbearing age congregate or represent a significant proportion of the work force. Such settings include day-care centers, schools, colleges, companies, government offices, and industrial sites.

#### **Vaccination for College Entry**

Colleges are high-risk areas for rubella transmission because of large concentrations of susceptible persons. Proof of rubella, as well as measles immunity, should be required for attendance for both male and female students.

#### **General Principles**

Voluntary programs have generally been less successful than mandatory programs. The military services require rubella immunity of susceptible recruits and have essentially eliminated rubella from military bases. In all settings where young adults congregate, males as well as females should be included, since males may transmit disease to susceptible females.

When practical, and when reliable laboratory services are available, potential female vaccinees of childbearing age can have serologic tests to determine susceptibility to rubella. However, with the exception of premarital and prenatal screening, routinely performing serologic tests for all women of childbearing age to determine susceptibility so that vaccine is given only to proven susceptible women is expensive and has been ineffective in some areas. Two visits to the health-care provider are necessary—one for screening and one for vaccination. Accordingly, the ACIP believes that rubella vaccination of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing and may be preferable, particularly when costs of serology are high and follow-up of identified susceptibles for vaccination is not assured. Vaccinated women should avoid becoming pregnant for a 3-month period following vaccination. In addition, vaccine should be administered in the above-mentioned settings only if there are no contraindications to vaccination.

Routine serologic screening of male vaccinees is not recommended. There are no conclusive data indicating that vaccination of immune individuals carries an increased risk of joint or other complications.

Health-care providers are encouraged to use MMR in routine childhood vaccination programs and whenever rubella vaccine is to be given to persons likely to be susceptible to measles and/or mumps as well as to rubella.

#### **Outbreak Control**

Outbreak control will play an important role in CRS elimination. Aggressive responses to outbreaks may interrupt chains of transmission and will increase immunization levels in persons who might otherwise not be vaccinated. Although methods for controlling rubella outbreaks are evolving, the major strategy should be to define target populations, ensure that susceptible individuals are vaccinated rapidly (or excluded from exposure if a contraindication exists), and maintain active surveillance to modify control measures if the situation changes.

Since a simple, accurate clinical case definition for rubella has not yet been developed, laboratory confirmation of cases is important. However, control measures should be implemented *before* serologic confirmation. This approach is especially important in any outbreak setting involving pregnant women (e.g., in obstetric-gynecologic and prenatal clinics). All persons who cannot readily provide laboratory evidence of immunity or a documented history of vaccination on or after the first-year birthday should be considered susceptible and vaccinated if there are no contraindications.

An effective means of terminating outbreaks and increasing rates of immunization quickly is to exclude from possible contact individuals who cannot provide valid evidence of immunity. Experience with measles-outbreak control indicates that almost all students who are excluded from school because they lack evidence of measles immunity quickly comply with requirements and are promptly readmitted to school. Exclusion should include all persons who have been exempted from rubella vaccination because of medical, religious, or other reasons. Exclusion should continue until 3 weeks after the onset of rash of the last reported case in the outbreak setting. Less rigorous approaches, such as voluntary appeals for vaccination, have not been effective in terminating outbreaks.

Mandatory exclusion and vaccination of adults should be practiced in rubella outbreaks in medical settings where large numbers of pregnant women may be exposed. This approach may be successful in terminating, or at least limiting, outbreaks. Vaccination during an outbreak has not been associated with significant personnel absenteeism. However, it is clear that vaccination of susceptible persons before an outbreak occurs is preferable, since vaccination causes far less absenteeism and disruption of routine work activities and schedules than rubella infection.

#### **SURVEILLANCE**

Surveillance of rubella and CRS has three purposes: (1) to provide important data on program progress and long-term trends; (2) to help define groups in greatest need of vaccination and in turn provide information for formulation of new strategies; and (3) to evaluate vaccine efficacy, duration of vaccine-induced immunity, and other issues related to vaccine safety and efficacy.

As the rates of rubella and CRS decline in the United States, effective surveillance becomes increasingly important. Known or suspected rubella cases should be reported immediately to local health departments. Since an accurate assessment of CRS elimination can be made only through aggressive case finding, surveillance of CRS will have to be intensified.

Surveillance of rubella is complicated by the fact that the clinical disease is not characteristic and can be confused with a number of other illnesses. Thus, there is a need for laboratory confirmation of cases, particularly in nonoutbreak settings. Similarly, laboratory confirmation of suspected cases of CRS is also necessary, since the constellation of findings of CRS may not be specific.

#### **Laboratory Diagnosis**

**Rubella:** Rubella infection can be serologically confirmed by a fourfold rise in HI or complement fixation (CF) antibody titer. Kits using EIA or latex agglutination assays are also becoming available for diagnostic use. The acute-phase serum specimen should be drawn as soon after rash onset as possible, preferably within the first 7 days. The convalescent-phase serum specimen should be drawn 10 or more days after the acute-phase serum specimen. If the acute-phase serum specimen is drawn more than 7 days after rash onset, a fourfold rise in HI antibody titer may not be detected. In this case, CF testing may be especially useful, since CF antibodies appear in serum later than HI antibodies. Both the acute and convalescent specimens should be tested simultaneously in the same laboratory.

Occasionally, fourfold rises may not be detected, even if the first specimen is drawn within the first 7 days after rash onset. Rubella infection may also be serologically confirmed by demonstrating rubella-specific IgM antibody. If IgM is to be determined, a single serum specimen should be drawn between 1 week and 2 weeks after rash onset. Although rubella-specific IgM antibody may be detected shortly after rash onset, false-negative results may occur if the specimen is drawn earlier than 1 week or later than 3 weeks following rash onset.

In the absence of rash illness, the diagnosis of subclinical cases of rubella can be facilitated by obtaining the acute-phase serum specimen as soon as possible after *exposure*. The convalescent-phase specimen should then be drawn 28 or more days after exposure. If acute- and convalescent-phase sera pairs provide inconclusive results, rubella-specific IgM antibody testing can be performed, but negative results should be interpreted cautiously. Expert consultation may be necessary to interpret the data.

Confirmation of rubella infection in pregnant women of unknown immune status following rash illness or exposure can frequently be difficult. A serum specimen should be obtained as soon as possible. Unfortunately, serologic results are often nonconfirmatory. Such situations can be minimized by performing prenatal serologies routinely. In addition, health providers should request that laboratories performing prenatal screening retain such specimens until delivery so that retesting, if necessary, can be done.

**Congenital Rubella:** Suspected cases of CRS should be managed with contact isolation (see CDC "Guidelines for Isolation Precautions in Hospitals") and, while diagnostic confirmation is pending, should be cared for only by personnel known to be immune. Confirmation by attempting virus isolation can be done using nasopharyngeal and urine specimens. Serologic confirmation can be obtained by testing cord blood for the presence of rubella-specific IgM antibodies. An alternative, but less rapid serologic method, is to document persistence of rubella-specific antibody in a suspected infant for more than 3 months of age at a level beyond that expected from passive transfer of maternal antibody (i.e., a rubella HI titer in the infant that does not decline at the expected



rate of one twofold dilution per month). If CRS is confirmed, precautions will need to be exercised through the first year of life, unless nasopharyngeal and urine cultures are negative for rubella virus.

#### Adverse Events

Continuous and careful review of adverse events following rubella vaccination is important. All adverse events following rubella vaccination should be evaluated and reported in detail through local and state health officials to CDC, as well as to the manufacturer.

#### INTERNATIONAL TRAVEL

Persons without evidence of rubella immunity who travel abroad should be protected against rubella, since rubella is endemic and even epidemic, in many countries throughout the world. No immunization or record of immunization is required for entry into the United States. However, it is recommended that international travelers have immunity to rubella consisting of laboratory evidence of rubella antibodies or verified rubella vaccination on or after the first-year birthday. It is especially important to protect susceptible women of childbearing age, particularly those planning to remain out of the country for a prolonged period of time.

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# IMPORTANT INFORMATION ABOUT MEASLES, MUMPS, AND RUBELLA AND MEASLES, MUMPS, AND RUBELLA VACCINES

*Please Read This Carefully*

MMR 1/1/88

## WHAT IS MEASLES?

Measles is the most serious of the common childhood diseases. Usually it causes a rash, high fever, cough, runny nose, and watery eyes lasting 1 to 2 weeks. Sometimes it is more serious. It causes an ear infection or pneumonia in nearly 1 out of 10 children who get it. Approximately 1 child out of every 1,000 who get measles has an inflammation of the brain (encephalitis). This can lead to convulsions, deafness, or mental retardation. About 2 children in every 10,000 who get measles die from it. Measles can also cause a pregnant woman to have a miscarriage or give birth to a premature baby.

Before measles vaccine shots were available, there were hundreds of thousands of cases and hundreds of deaths each year. Nearly all children got measles by the time they were 15. Now, wide use of measles vaccine has nearly eliminated measles from the United States. However, if children are not vaccinated they have a high risk of getting measles, either now or later in life.

## WHAT IS MUMPS?

Mumps is a common disease of children. Usually it causes fever, headache, and inflammation of the salivary glands, which causes the cheeks to swell. Sometimes it is more serious. It causes a mild inflammation of the coverings of the brain and spinal cord (meningitis) in about 1 child in every 10 who get it. More rarely, it can cause inflammation of the brain (encephalitis) which usually goes away without leaving permanent damage. Mumps can also cause deafness. About 1 out of every 4 adolescent or adult men who get mumps develops painful inflammation and swelling of the testicles. While this condition usually goes away, on rare occasions it may cause sterility. Before mumps vaccine shots were available, there were more than 150,000 cases each year. Now, because of the wide use of mumps vaccine, the number of cases of mumps is much lower. However, if children are not vaccinated, they have a high risk of getting mumps.

## WHAT IS RUBELLA?

Rubella is also called German measles. It is a common disease of children and

may also affect adults. Usually it is very mild and causes a slight fever, rash, and swelling of glands in the neck. The sickness lasts about 3 days. Sometimes, especially in adult women, there may be swelling and aching of the joints for a week or two. Very rarely, rubella can cause inflammation of the brain (encephalitis) or cause a temporary bleeding disorder (purpura).

The most serious problem with rubella is that if a pregnant woman gets this disease, there is a good chance that she may have a miscarriage or that the baby will be born crippled, blind, or with other defects. The last big rubella epidemic in the United States was in 1964. Because of that epidemic, about 20,000 children were born with serious problems such as heart defects, deafness, blindness, or mental retardation because their mothers had rubella during the pregnancy.

Before rubella vaccine shots were available, rubella was so common that most children got the disease by the time they were 15. Now, because of the wide use of rubella vaccine, the number of cases of rubella is much lower. However, if children are not immunized, they have a high risk of getting rubella and possibly exposing a pregnant woman to the disease. If an unimmunized woman later becomes pregnant and catches rubella, she may have a defective baby. Since rubella is a mild illness, many women of childbearing age do not recall if they had rubella as a child. A simple blood test can show whether a person is immune to rubella or is not protected against the disease. Overall, about 1 in 5 women of childbearing age is not protected against rubella.

## MEASLES, MUMPS, AND RUBELLA VACCINES:

The vaccines are given by injection and are very effective. Ninety percent or more of people who get the shot will have protection, probably for life. Since protection is not as likely to occur if the vaccines are given very early in life, these vaccines should be given to children after their first birthday; measles vaccine should be given at 15 months of age or older. Measles, mumps, and rubella vaccines can be given one at a time or in a combined vaccine

*(PLEASE READ OTHER SIDE)*

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Helena, MT 59620

(measles-rubella [MR], measles-mumps-rubella [MMR]) by a single shot. If they are given in combined vaccine, they should be given at 15 months of age or older.

Experts recommend that adolescents and adults—especially women of child-bearing age—who are not known to be immune to rubella should receive rubella vaccine (or MMR if they might also be susceptible to measles or mumps). Women should not receive the shot if they are pregnant or might become pregnant within 3 months. There is no known risk in being immunized against any or all three of these diseases if you are already immune to any of them.

#### POSSIBLE SIDE EFFECTS FROM THE VACCINES:

About 1 out of every 5 children will get a rash or slight fever lasting for a few days, 1 or 2 weeks after getting measles vaccine. Occasionally there is mild swelling of the salivary glands after mumps vaccination.

About 1 out of every 7 children who get rubella vaccine will get a rash or some swelling of the glands of the neck 1 or 2 weeks after the shot. About 1 out of every 20 children who get rubella vaccine will have some aching or swelling of the joints. This may happen anywhere from 1-3 weeks after the shot. It usually lasts only 2 or 3 days. Adults are more likely to have these problems with their joints—as many as 4 in 10 may have them. True arthritis with swelling of the joints is generally seen in less than two percent of adults receiving rubella vaccine. If pain or swelling of the joints occurs, it rarely lasts for more than a few days and rarely returns. Other temporary side effects, such as pain, numbness, or tingling in the hands and feet have also occurred but are very uncommon.

Although experts are not sure, it seems that very rarely children who get these vaccines may have a more serious reaction, such as inflammation of the brain (encephalitis), convulsions with fever, or nerve deafness.

With any vaccine or drug, there is a possibility that allergic or other more serious reactions or even death could occur.

#### PERSONAL OR FAMILY HISTORY OF CONVULSIONS:

Children who have had a convulsion and children who have a brother, sister, or parent who has ever had a convulsion are more likely to have a convulsion after receiving measles vaccine. Advisory committees of the United States Public Health Service and the American Academy of Pediatrics recommend that because of the overall risk of measles disease and the fact that the risk

of convulsions is still very low, children with a personal history of a convulsion and children with a family history of convulsions should receive measles vaccine. However, you should tell the person who is to give the immunization about such a history and discuss the possibility of using an anti-fever medicine.

#### WARNING—SOME PERSONS SHOULD NOT TAKE THESE VACCINES WITHOUT CHECKING WITH A DOCTOR:

- Anyone who is sick right now with something more serious than a cold.
- Anyone who had an allergic reaction to eating eggs so serious that it required medical treatment (does not apply to rubella vaccine).
- Anyone with cancer, leukemia, or lymphoma.
- Anyone with a disease that lowers the body's resistance to infection.
- Anyone taking a drug that lowers the body's resistance to infection (such as cortisone, prednisone or certain anticancer drugs).
- Anyone who has received gamma globulin (immune globulin) within the preceding 3 months.
- Anyone who had an allergic reaction to an antibiotic called neomycin so serious that it required medical treatment.

#### PREGNANCY:

Measles, mumps, and rubella vaccines are not known to cause special problems for pregnant women or their unborn babies. However, doctors usually avoid giving any drugs or vaccines to pregnant women unless there is a specific need. To be safe, pregnant women should not get these vaccines. A woman who gets any of these vaccines should wait 3 months before getting pregnant.

Immunizing a child whose mother is pregnant is not dangerous to the pregnancy.

#### QUESTIONS:

If you have any questions about measles, mumps, or rubella immunization, please ask us now or call your doctor or health department before you sign this form.

#### REACTIONS:

If the person who received the vaccine has a convulsion or other serious reaction the person should be seen promptly by a doctor.

If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after immunization, please report it to:

### PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

*I have read or have had explained to me the information on this form about measles, mumps, and rubella and measles, mumps, and rubella vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of measles, mumps, and rubella vaccine and request that the vaccine checked below be given to me or to the person named below for whom I am authorized to make this request.*

Vaccine to be given:  Measles  Mumps  
 Rubella  Measles-Rubella  Measles-Mumps-Rubella

MMR 1/1/88

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                       |            |       |           |      |
|--|------------|-------|-----------|------|
| Last Name  | First Name | MI    | Birthdate | Age  |
| Address  |            |       |           |      |
| City   | County     | State | Zip       |      |
| Signature of person to receive vaccine or person authorized to make the request. |            |       |           | Date |

| FOR CLINIC USE     |
|--------------------|
| Clinic Ident.      |
| Date Vaccinated    |
| Manuf. and Lot No. |
| Site of Injection  |

| FOR DATA PROCESSING USE ONLY (OPTIONAL)  |                          |                          |                          |                          |                          |          |                          |                |                          |
|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|----------|--------------------------|----------------|--------------------------|
| VACCINE HISTORY: PLACE CHECK <input type="checkbox"/> IN BOX IF HISTORY PREVIOUSLY SUBMITTED |                          |                          |                          |                          |                          |          |                          |                |                          |
| DTP:   | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | MEASLES: | <input type="checkbox"/> | MUMPS:         | <input type="checkbox"/> |
| POLIO:   | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | RUBELLA: | <input type="checkbox"/> | HAEMOPHILUS b: | <input type="checkbox"/> |

Mumps

VACCINE AVAILABILITY

The Immunization Program provides mumps vaccine in combination with measles and rubella vaccine (MMR).

See the attached ACIP statement and Important Information Form. Also, refer to the Adult Immunization Recommendation on Mumps and the Control of Communicable Diseases in Man.



Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Mumps Prevention**

*This revised Immunization Practices Advisory Committee (ACIP) recommendation on mumps vaccine updates the 1982 recommendation (1). Changes include: a discussion of the evolving epidemiologic characteristics of mumps, introduction of a cutoff of 1957 as the oldest birth cohort for which mumps vaccination is routinely recommended, and more aggressive outbreak-control measures. Although there are no major changes in vaccination strategy, these revised recommendations place a greater emphasis on vaccinating susceptible adolescents and young adults.*

**INTRODUCTION**

**Mumps Disease**

Mumps disease is generally self-limited, but it may be moderately debilitating. Naturally acquired mumps infection, including the estimated 30% of infections that are subclinical, confers long-lasting immunity.

Among the reported mumps-associated complications, strong epidemiologic and laboratory evidence for an association with meningoencephalitis, deafness, and orchitis has been reported (2). Meningeal signs appear in up to 15% of cases. Reported rates of mumps encephalitis range as high as five cases per 1000 reported mumps cases. Permanent sequelae are rare, but the reported encephalitis case-fatality rate has averaged 1.4%. Although overall mortality is low, death due to mumps infection is much more likely to occur in adults; about half of mumps-associated deaths have been in persons  $\geq 20$  years old (2). Sensorineural deafness is one of the most serious of the rare complications involving the central nervous system (CNS). It occurs with an estimated frequency of 0.5-5.0 per 100,000 reported mumps cases. Orchitis (usually unilateral) has been reported as a complication in 20%-30% of clinical mumps cases in postpubertal males (3). Some testicular atrophy occurs in about 35% of cases of mumps orchitis, but sterility rarely occurs. Symptomatic involvement of other organs has been observed less frequently. There are limited experimental, clinical, and epidemiologic data that suggest permanent pancreatic damage may result from injury caused by direct viral invasion. Further research is needed to determine whether mumps infection contributes to the pathogenesis of diabetes mellitus. Mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion (reported to be as high as 27%). There is no evidence that mumps during pregnancy causes congenital malformations.

**Epidemiology**

Following the introduction of the live mumps virus vaccine in 1967 and recommendation of its routine use in 1977, the incidence rate of reported mumps cases decreased steadily in the United States. In 1985, a record low of 2982 cases was reported, representing a 98% decline from the 185,691 cases reported in 1967. However, between 1985 and 1987, a relative resurgence of mumps occurred, with 7790 cases reported in 1986 and 12,848 cases in 1987 (4). During this 3-year period, the annual reported incidence rate rose almost fivefold, from 1.1 cases per 100,000 population to 5.2 cases per 100,000 population. In 1988, a provisional total of 4730 cases was reported, representing a 62% decrease from 1987.

As in the prevaccine era, the majority of reported mumps cases still occur in school-aged children (5-14 years of age). Almost 60% of reported cases occurred in this population between 1985 and 1987, compared with an average of 75% of reported cases between 1967 and 1971, the first 5-year period postlicensure. However, for the first time since mumps became a reportable disease, the reported peak incidence rate shifted from 5-9-year-olds to older age groups for two consecutive years (1986 and 1987). Persons  $\geq 15$  years of age accounted for more than one third of the reported total between 1985 and 1987; in 1967-1971, an average of only 8% of reported cases occurred among this population.

Although reported mumps incidence increased in all age groups from 1985 to 1987, the most dramatic increases were among 10–14-year-olds (almost a sevenfold increase) and 15–19-year-olds (more than an eightfold increase).

The increased occurrence of mumps in susceptible adolescents and young adults has been demonstrated in several recent outbreaks in high schools and on college campuses (5,6) and in occupational settings (7). Nonetheless, despite this age shift in reported mumps, the overall reported risk of disease in persons 10–14 and  $\geq 15$  years of age is still lower than that in the prevaccine and early postvaccine era.

Consistent with previous findings (8), reported incidence rates are lower in states with comprehensive school immunization laws. The District of Columbia and 14 states that routinely reported mumps cases in 1987 had comprehensive laws that require proof of immunity against mumps for school attendance from kindergarten through grade 12 (K–12). In these 15 areas, the incidence rate in 1987 was 1.1 mumps cases per 100,000 population. In contrast, among the other states that routinely reported mumps cases in 1987, mumps incidence was highest in the 14 states without requirements for mumps vaccination (11.5 cases per 100,000 population), and intermediate (6.2 cases per 100,000 population) in the 18 states with partial vaccination requirements for school attendance (i.e., those that include some children but do not comprehensively include K–12). Furthermore, the shift in age-specific risk noted above occurred only in states without comprehensive K–12 school vaccination requirements.

Both the shift in risk to older persons and the relative resurgence of reported mumps activity noted in recent years are attributable to the relatively underimmunized cohort of children born between 1967 and 1977 (9). There is no evidence of waning immunity in vaccinated persons. During 1967–1977, the risk of exposure to mumps declined rapidly even though vaccination of children against mumps was only gradually being accepted as a routine practice. Simultaneously, mumps vaccine coverage did not reach levels  $>50\%$  in any age group until 1976 (5–9-year-olds); in persons 15–19 years old, vaccine coverage did not reach these levels until 1983. This lag in coverage relative to measles and rubella vaccines reflects the lack of an ACIP recommendation for routine mumps vaccine until 1977 and the lack of emphasis in ACIP recommendations on vaccination beyond toddler age until 1980. These facts and the observed shift in risk to older persons in states without comprehensive mumps immunization school laws provide further evidence that a failure to vaccinate, rather than vaccine failure, is primarily responsible for the recently observed changes in mumps occurrence.

#### **MUMPS VIRUS VACCINE**

A killed mumps virus vaccine was licensed for use in the United States from 1950 through 1978. This vaccine induced antibody, but the immunity was transient. The number of doses of killed mumps vaccine administered between licensure of live attenuated mumps vaccine in 1967 until 1978 is unknown but appears to have been limited.

Mumps virus vaccine\* is prepared in chick-embryo cell culture. More than 84 million doses were distributed in the United States from its introduction in December 1967 through 1988. The vaccine produces a subclinical, noncommunicable infection with very few side effects. Mumps vaccine is available both in monovalent (mumps only) form and in combinations: mumps-rubella and measles-mumps-rubella (MMR) vaccines.

The vaccine is approximately 95% efficacious in preventing mumps disease (10,11);  $>97\%$  of persons known to be susceptible to mumps develop measurable antibody following vaccination (12). Vaccine-induced antibody is protective and long-lasting (13,14), although of considerably lower titer than antibody resulting from natural infection (12). The duration of vaccine-induced immunity is unknown, but serologic and epidemiologic data collected during 20 years of live vaccine use indicate both the persistence of antibody and continuing protection against infection. Estimates of clinical vaccine efficacy ranging from 75% to 95% have been calculated from data collected in outbreak settings using different epidemiologic study designs (8,15).

#### **Vaccine Shipment and Storage**

Administration of improperly stored vaccine may fail to protect against mumps. During storage before reconstitution, mumps vaccine must be kept at 2–8 C (35.6–46.4 F) or colder. It must also be protected from light, which may inactivate the virus. Vaccine must be shipped at 10 C (50 F) or colder and may be shipped on dry ice. After reconstitution, the vaccine should be stored in a dark place at 2–8 C (35.6–46.4 F) and discarded if not used within 8 hours.

\*Official name: Mumps Virus Vaccine, Live.



## VACCINE USAGE

(See also the current ACIP statement, "General Recommendations on Immunization" [16].)

### General Recommendations

Susceptible children, adolescents, and adults should be vaccinated against mumps, unless vaccination is contraindicated. Mumps vaccine is of particular value for children approaching puberty and for adolescents and adults who have not had mumps. MMR vaccine is the vaccine of choice for routine administration and should be used in all situations where recipients are also likely to be susceptible to measles and/or rubella. The favorable benefit-cost ratio for routine mumps immunization is more marked when vaccine is administered as MMR (17). Persons should be considered susceptible to mumps unless they have documentation of 1) physician-diagnosed mumps, 2) adequate immunization with live mumps virus vaccine on or after their first birthday, or 3) laboratory evidence of immunity. Because live mumps vaccine was not used routinely before 1977 and because the peak age-specific incidence was in 5-9-year-olds before the vaccine was introduced, most persons born before 1957 are likely to have been infected naturally between 1957 and 1977. Therefore, they generally may be considered to be immune, even if they may not have had clinically recognizable mumps disease. However, this cutoff date for susceptibility is arbitrary. Although outbreak-control efforts should be focused on persons born after 1956, these recommendations do not preclude vaccination of possibly susceptible persons born before 1957 who may be exposed in outbreak settings.

Persons who are unsure of their mumps disease history and/or mumps vaccination history should be vaccinated. There is no evidence that persons who have previously either received mumps vaccine or had mumps are at any increased risk of local or systemic reactions from receiving live mumps vaccine. Testing for susceptibility before vaccination, especially among adolescents and young adults, is not necessary. In addition to the expense, some tests (e.g., mumps skin test and the complement-fixation antibody test) may be unreliable, and tests with established reliability (neutralization, enzyme immunoassay, and radial hemolysis antibody tests) are not readily available.

**Dosage.** A single dose of vaccine in the volume specified by the manufacturer should be administered subcutaneously. While not recommended routinely, intramuscular vaccination is effective and safe.

**Age.** Live mumps virus vaccine is recommended at any age on or after the first birthday for all susceptible persons, unless a contraindication exists. Under routine circumstances, mumps vaccine should be given in combination with measles and rubella vaccines as MMR, following the currently recommended schedule for administration of measles vaccine. It should not be administered to infants <12 months old because persisting maternal antibody might interfere with seroconversion. To insure immunity, all persons vaccinated before the first birthday should be revaccinated on or after the first birthday.

### Persons Exposed to Mumps

**Use of Vaccine.** When given after exposure to mumps, live mumps virus vaccine may not provide protection. However, if the exposure did not result in infection, vaccine should induce protection against infection from subsequent exposures. There is no evidence that the risk of vaccine-associated adverse events increases if vaccine is administered to persons incubating disease.

**Use of Immune Globulin.** Immune globulin (IG) has not been demonstrated to be of established value in postexposure prophylaxis and is not recommended. Mumps immune globulin has not been shown to be effective and is no longer available or licensed for use in the United States.

### Adverse Effects of Vaccine Use

In field trials before licensure, illnesses did not occur more often in vaccinees than in unvaccinated controls (18). Reports of illnesses following mumps vaccination have mainly been episodes of parotitis and low-grade fever. Allergic reactions including rash, pruritus, and purpura have been temporally associated with mumps vaccination but are uncommon and usually mild and of brief duration. The reported occurrence of encephalitis within 30 days of receipt of a mumps-containing vaccine (0.4 per million doses) is not greater than the observed background incidence rate of CNS dysfunction in the normal population. Other manifestations of CNS involvement, such as febrile seizures and deafness, have also been infrequently reported. Complete recovery is usual. Reports of nervous system illness following mumps vaccination do not necessarily denote an etiologic relationship between the illness and the vaccine.

### Contraindications to Vaccine Use

**Pregnancy.** Although mumps vaccine virus has been shown to infect the placenta and fetus (19), there is no evidence that it causes congenital malformations in humans. However, because of the

theoretical risk of fetal damage, it is prudent to avoid giving live virus vaccine to pregnant women. Vaccinated women should avoid pregnancy for 3 months after vaccination. Routine precautions for vaccinating postpubertal women include asking if they are or may be pregnant, excluding those who say they are, and explaining the theoretical risk to those who plan to receive the vaccine. Vaccination during pregnancy should not be considered an indication for termination of pregnancy. However, the final decision about interruption of pregnancy must rest with the individual patient and her physician.

**Severe Febrile Illness.** Vaccine administration should not be postponed because of minor or intercurrent febrile illnesses, such as mild upper respiratory infections. However, vaccination of persons with severe febrile illnesses should generally be deferred until they have recovered.

**Allergies.** Because live mumps vaccine is produced in chick-embryo cell culture, persons with a history of anaphylactic reactions (hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) after egg ingestion should be vaccinated only with caution using published protocols (20,21). Known allergic children should not leave the vaccination site for 20 minutes. Evidence indicates that persons are not at increased risk if they have egg allergies that are not anaphylactic in nature. Such persons may be vaccinated in the usual manner. There is no evidence to indicate that persons with allergies to chickens or feathers are at increased risk of reaction to the vaccine.

Since mumps vaccine contains trace amounts of neomycin (25 µg), persons who have experienced anaphylactic reactions to topically or systemically administered neomycin should not receive mumps vaccine. Most often, neomycin allergy is manifested as a contact dermatitis, which is a delayed-type (cell-mediated) immune response, rather than anaphylaxis. In such persons, the adverse reaction, if any, to 25 µg of neomycin in the vaccine would be an erythematous, pruritic nodule or papule at 48-96 hours. A history of contact dermatitis to neomycin is not a contraindication to receiving mumps vaccine. Live mumps virus vaccine does not contain penicillin.

**Recent IG Injection.** Passively acquired antibody can interfere with the response to live, attenuated-virus vaccines. Therefore, mumps vaccine should be given at least 2 weeks before the administration of IG or deferred until approximately 3 months after the administration of IG.

**Altered Immunity.** In theory, replication of the mumps vaccine virus may be potentiated in patients with immune deficiency diseases and by the suppressed immune responses that occur with leukemia, lymphoma, or generalized malignancy or with therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. In general, patients with such conditions should not be given live mumps virus vaccine. Because vaccinated persons do not transmit mumps vaccine virus, the risk of mumps exposure for those patients may be reduced by vaccinating their close susceptible contacts.

An exception to these general recommendations is in children infected with human immunodeficiency virus (HIV); all asymptomatic HIV-infected children should receive MMR at 15 months of age (22). If measles vaccine is administered to symptomatic HIV-infected children, the combination MMR vaccine is generally preferred (23).

Patients with leukemia in remission whose chemotherapy has been terminated for at least 3 months may also receive live mumps virus vaccine. Short-term (<2 weeks' duration) corticosteroid therapy, topical steroid therapy (e.g., nasal, skin), and intraarticular, bursal, or tendon injection with corticosteroids do not contraindicate mumps vaccine administration. However, mumps vaccine should be avoided if systemic immunosuppressive levels are reached by prolonged, extensive, topical application.

**Other.** There is no known association between mumps vaccination and pancreatic damage or subsequent development of diabetes mellitus (24).

#### **MUMPS CONTROL**

The principal strategy to prevent mumps is to achieve and maintain high immunization levels, primarily in infants and young children. Universal immunization as a part of good health care should be routinely carried out in physicians' offices and public health clinics. Programs aimed at vaccinating children with MMR should be established and maintained in all communities. In addition, other persons thought to be susceptible should be vaccinated unless otherwise contraindicated. This is especially important for adolescents and young adults in light of the recently observed increase in risk of disease in these populations.

Because access to some population subgroups is limited, the ACIP recommends taking maximal advantage of clinic visits to vaccinate susceptible persons ≥15 months of age by administering MMR, diphtheria-tetanus-pertussis (DTP), and oral polio vaccine (OPV) simultaneously if all are needed. Health agencies should take necessary steps, including the development, adoption, and enforcement

of comprehensive immunization requirements, to ensure that all persons in schools at all grade levels and in day-care settings are protected against mumps. Similar requirements should be considered for colleges, as recommended by the American College Health Association (25), and selected places of employment where persons in this age cohort are likely to be concentrated or where the consequences of disease spread may be more severe (e.g., medical-care settings).

In determining means to control mumps outbreaks, exclusion of susceptible students from affected schools and schools judged by local public health authorities to be at risk for transmission should be considered. Such exclusion should be an effective means of terminating school outbreaks and quickly increasing rates of immunization. Excluded students can be readmitted immediately after vaccination. Pupils who have been exempted from mumps vaccination because of medical, religious, or other reasons should be excluded until at least 28 days after the onset of parotitis in the last person with mumps in the affected school. Experience with outbreak control for other vaccine-preventable diseases indicates that almost all students who are excluded from the outbreak area because they lack evidence of immunity quickly comply with requirements and can be readmitted to school.

#### **MUMPS DISEASE SURVEILLANCE AND REPORTING OF ADVERSE EVENTS**

There is a continuing need to improve the reporting of mumps cases and complications and to document the duration of vaccine effectiveness. Thus, for areas in which mumps is a reportable disease, all suspected cases of mumps should be reported to local or state health officials.

The National Childhood Vaccine Injury Compensation Program established by the National Childhood Vaccine Injury Compensation Act of 1986 requires physicians and other health-care providers who administer vaccines to maintain permanent immunization records and to report occurrences of certain adverse events to the U.S. Department of Health and Human Services. Recording and reporting requirements took effect on March 21, 1988. Reportable adverse events include those listed in the Act for mumps (26) and events specified in the manufacturer's vaccine package insert as contraindications to further doses of mumps vaccine.

Although there eventually will be one system for reporting adverse events following immunizations, two separate systems currently exist. The appropriate reporting method currently depends on the source of funding used to purchase the vaccine (26). Events that occur after receipt of a vaccine purchased with public (federal, state, and/or local government) funds must be reported by the administering health provider to the appropriate local, county, or state health department. The state health department completes and submits the correct forms to CDC. Reportable events that follow administration of vaccines purchased with private money are reported by the health-care provider directly to the Food and Drug Administration.

#### **RECOMMENDATIONS FOR INTERNATIONAL TRAVEL**

Mumps is still endemic throughout most of the world. While vaccination against mumps is not a requirement for entry into any country, susceptible children, adolescents, and adults would benefit by being vaccinated with a single dose of vaccine (usually as MMR), unless contraindicated, before beginning travel. Because of concern about inadequate seroconversion due to persisting maternal antibodies and because the risk of serious disease from mumps infection is relatively low, persons <12 months of age need not be given mumps vaccine before travel.

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# IMPORTANT INFORMATION ABOUT MEASLES, MUMPS, AND RUBELLA AND MEASLES, MUMPS, AND RUBELLA VACCINES

*Please Read This Carefully*

MMR 1/1/88

## WHAT IS MEASLES?

Measles is the most serious of the common childhood diseases. Usually it causes a rash, high fever, cough, runny nose, and watery eyes lasting 1 to 2 weeks. Sometimes it is more serious. It causes an ear infection or pneumonia in nearly 1 out of 10 children who get it. Approximately 1 child out of every 1,000 who get measles has an inflammation of the brain (encephalitis). This can lead to convulsions, deafness, or mental retardation. About 2 children in every 10,000 who get measles die from it. Measles can also cause a pregnant woman to have a miscarriage or give birth to a premature baby.

Before measles vaccine shots were available, there were hundreds of thousands of cases and hundreds of deaths each year. Nearly all children got measles by the time they were 15. Now, wide use of measles vaccine has nearly eliminated measles from the United States. However, if children are not vaccinated they have a high risk of getting measles, either now or later in life.

## WHAT IS MUMPS?

Mumps is a common disease of children. Usually it causes fever, headache, and inflammation of the salivary glands, which causes the cheeks to swell. Sometimes it is more serious. It causes a mild inflammation of the coverings of the brain and spinal cord (meningitis) in about 1 child in every 10 who get it. More rarely, it can cause inflammation of the brain (encephalitis) which usually goes away without leaving permanent damage. Mumps can also cause deafness. About 1 out of every 4 adolescent or adult men who get mumps develops painful inflammation and swelling of the testicles. While this condition usually goes away, on rare occasions it may cause sterility. Before mumps vaccine shots were available, there were more than 150,000 cases each year. Now, because of the wide use of mumps vaccine, the number of cases of mumps is much lower. However, if children are not vaccinated, they have a high risk of getting mumps.

## WHAT IS RUBELLA?

Rubella is also called German measles. It is a common disease of children and

may also affect adults. Usually it is very mild and causes a slight fever, rash, and swelling of glands in the neck. The sickness lasts about 3 days. Sometimes, especially in adult women, there may be swelling and aching of the joints for a week or two. Very rarely, rubella can cause inflammation of the brain (encephalitis) or cause a temporary bleeding disorder (purpura).

The most serious problem with rubella is that if a pregnant woman gets this disease, there is a good chance that she may have a miscarriage or that the baby will be born crippled, blind, or with other defects. The last big rubella epidemic in the United States was in 1964. Because of that epidemic, about 20,000 children were born with serious problems such as heart defects, deafness, blindness, or mental retardation because their mothers had rubella during the pregnancy.

Before rubella vaccine shots were available, rubella was so common that most children got the disease by the time they were 15. Now, because of the wide use of rubella vaccine, the number of cases of rubella is much lower. However, if children are not immunized, they have a high risk of getting rubella and possibly exposing a pregnant woman to the disease. If an unimmunized woman later becomes pregnant and catches rubella, she may have a defective baby. Since rubella is a mild illness, many women of childbearing age do not recall if they had rubella as a child. A simple blood test can show whether a person is immune to rubella or is not protected against the disease. Overall, about 1 in 5 women of childbearing age is not protected against rubella.

## MEASLES, MUMPS, AND RUBELLA VACCINES:

The vaccines are given by injection and are very effective. Ninety percent or more of people who get the shot will have protection, probably for life. Since protection is not as likely to occur if the vaccines are given very early in life, these vaccines should be given to children after their first birthday; measles-vaccine should be given at 15 months of age or older. Measles, mumps, and rubella vaccines can be given one at a time or in a combined vaccine

*(PLEASE READ OTHER SIDE)*

Forms provided by: Montana Immunization Program  
Dept. of Health & Environmental Sciences  
Helena, MT 59620

(measles-rubella [MR], measles-mumps-rubella [MMR] by a single shot. If they are given in combined vaccine, they should be given at 15 months of age or older.

Experts recommend that adolescents and adults—especially women of child-bearing age—who are not known to be immune to rubella should receive rubella vaccine (or MMR if they might also be susceptible to measles or mumps). Women should not receive the shot if they are pregnant or might become pregnant within 3 months. There is no known risk in being immunized against any or all three of these diseases if you are already immune to any of them.

#### POSSIBLE SIDE EFFECTS FROM THE VACCINES:

About 1 out of every 5 children will get a rash or slight fever lasting for a few days, 1 or 2 weeks after getting measles vaccine. Occasionally there is mild swelling of the salivary glands after mumps vaccination.

About 1 out of every 7 children who get rubella vaccine will get a rash or some swelling of the glands of the neck 1 or 2 weeks after the shot. About 1 out of every 20 children who get rubella vaccine will have some aching or swelling of the joints. This may happen anywhere from 1-3 weeks after the shot. It usually lasts only 2 or 3 days. Adults are more likely to have these problems with their joints—as many as 4 in 10 may have them. True arthritis with swelling of the joints is generally seen in less than two percent of adults receiving rubella vaccine. If pain or swelling of the joints occurs, it rarely lasts for more than a few days and rarely returns. Other temporary side effects, such as pain, numbness, or tingling in the hands and feet have also occurred but are very uncommon.

Although experts are not sure, it seems that very rarely children who get these vaccines may have a more serious reaction, such as inflammation of the brain (encephalitis), convulsions with fever, or nerve deafness.

With any vaccine or drug, there is a possibility that allergic or other more serious reactions or even death could occur.

#### PERSONAL OR FAMILY HISTORY OF

##### CONVULSIONS:

Children who have had a convulsion and children who have a brother, sister, or parent who has ever had a convulsion are more likely to have a convulsion after receiving measles vaccine. Advisory committees of the United States Public Health Service and the American Academy of Pediatrics recommend that because of the overall risk of measles disease and the fact that the risk of

convulsions is still very low, children with a personal history of a convulsion and children with a family history of convulsions should receive measles vaccine. However, you should tell the person who is to give the immunization about such a history and discuss the possibility of using an anti-fever medicine.

#### WARNING—SOME PERSONS SHOULD NOT TAKE THESE VACCINES WITHOUT CHECKING WITH A DOCTOR:

- Anyone who is sick right now with something more serious than a cold.
- Anyone who had an allergic reaction to eating eggs so serious that it required medical treatment (does not apply to rubella vaccine).
- Anyone with cancer, leukemia, or lymphoma.
- Anyone with a disease that lowers the body's resistance to infection.
- Anyone taking a drug that lowers the body's resistance to infection (such as cortisone, prednisone or certain anticancer drugs).
- Anyone who has received gamma globulin (immune globulin) within the preceding 3 months.
- Anyone who had an allergic reaction to an antibiotic called neomycin so serious that it required medical treatment.

#### PREGNANCY:

Measles, mumps, and rubella vaccines are not known to cause special problems for pregnant women or their unborn babies. However, doctors usually avoid giving any drugs or vaccines to pregnant women unless there is a specific need. To be safe, pregnant women should not get these vaccines. A woman who gets any of these vaccines should wait 3 months before getting pregnant.

Immunizing a child whose mother is pregnant is not dangerous to the pregnancy.

#### QUESTIONS:

If you have any questions about measles, mumps, or rubella immunization, please ask us now or call your doctor or health department before you sign this form.

#### REACTIONS:

If the person who received the vaccine has a convulsion or other serious reaction the person should be seen promptly by a doctor.

If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic in the 4 weeks after immunization, please report it to:

### PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

*I have read or have had explained to me the information on this form about measles, mumps, and rubella and measles, mumps, and rubella vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of measles, mumps, and rubella vaccine and request that the vaccine checked below be given to me or to the person named below for whom I am authorized to make this request.*

Vaccine to be given:  Measles  Mumps  
 Rubella  Measles-Rubella  Measles-Mumps-Rubella

MMR 1/1/88

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                      |            |        |           |     |
|---|------------|--------|-----------|-----|
| Last Name   | First Name | MI     | Birthdate | Age |
| Address   |            |        |           |     |
| City  |            | County | State     | Zip |
| Signature of person to receive vaccine or person authorized to make the request |            |        |           |     |
| Date  |            |        |           |     |

| FOR CLINIC USE     |
|--------------------|
| Clinic Ident.      |
| Date Vaccinated    |
| Manuf. and Lot No. |
| Site of Injection  |

#### FOR DATA PROCESSING USE ONLY (OPTIONAL)

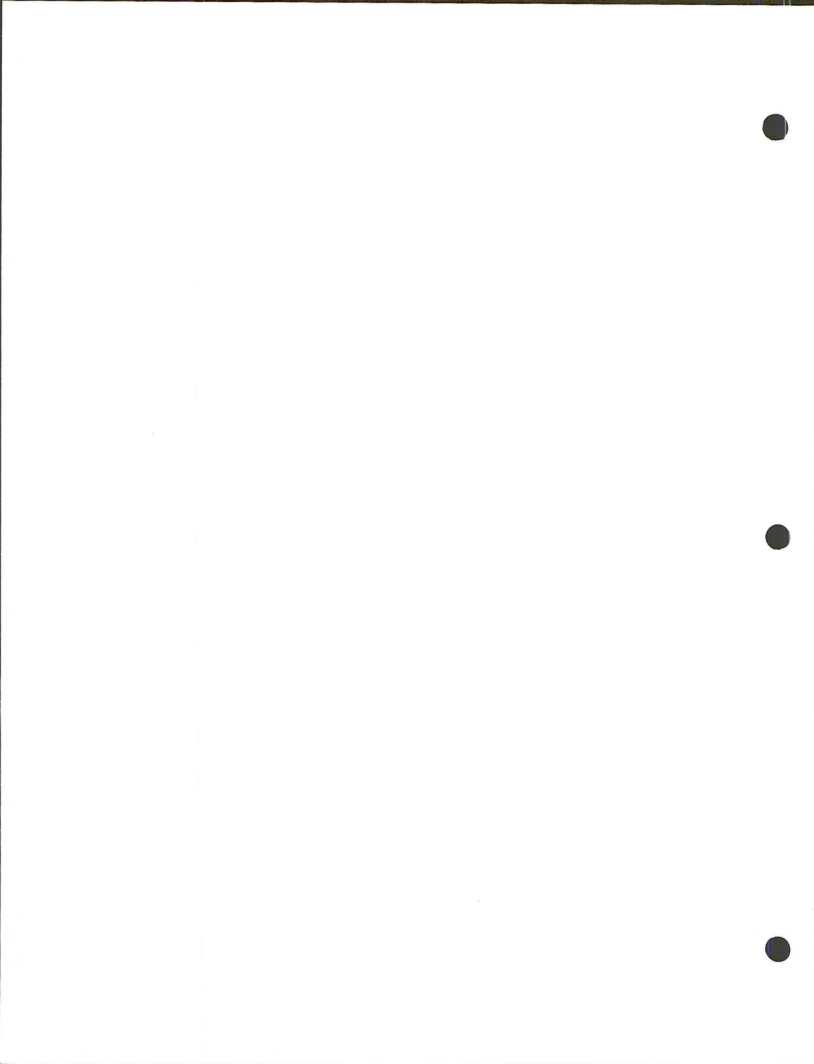
| VACCINE HISTORY: | PLACE CHECK              | IN BOX IF HISTORY PREVIOUSLY SUBMITTED |        |        |        |        |                 |                       |
|------------------|--------------------------|--|--------|--------|--------|--------|-----------------|-----------------------|
| DTP:             | <input type="checkbox"/> | m/d/yr                                 | m/d/yr | m/d/yr | m/d/yr | m/d/yr | MEASLES: m/d/yr | MUMPS: m/d/yr         |
| POLIO:           | <input type="checkbox"/> | m/d/yr                                 | m/d/yr | m/d/yr | m/d/yr | m/d/yr | RUBELLA: m/d/yr | HAEMOPHILUS b: m/d/yr |

Haemophilus Influenza Type b

VACCINE AVAILABILITY

The Immunization Program supplies Haemophilus b vaccine to public clinics.

See the attached ACIP statement and Important Information Form. Also, refer to the Control of Communicable Diseases in Man.





Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**Polysaccharide Vaccine for Prevention  
of *Haemophilus influenzae* Type b Disease**

**INTRODUCTION**

A polysaccharide vaccine\* against invasive (bacteremic) disease caused by *Haemophilus influenzae* type b recently has been licensed in the United States. The purposes of this statement are to summarize available information about this vaccine and to offer guidelines for its use in the prevention of invasive *H. influenzae* type b disease.

**HAEMOPHILUS INFLUENZAE DISEASE**

*H. influenzae* is a leading cause of serious systemic bacterial disease in the United States. It is the most common cause of bacterial meningitis, accounting for an estimated 12,000 cases annually, primarily among children under 5 years of age. The mortality rate is 5%, and neurologic sequelae are observed in as many as 25%-35% of survivors. Virtually all cases of *H. influenzae* meningitis among children are caused by strains of type b (Hib), although this capsular type represents only one of the six types known for this species. In addition to bacterial meningitis, Hib is responsible for other invasive diseases, including epiglottitis, sepsis, cellulitis, septic arthritis, osteomyelitis, pericarditis, and pneumonia. Nontypeable (noncapsulated) strains of *H. influenzae* commonly colonize the human respiratory tract and are a major cause of otitis media and respiratory mucosal infection but rarely result in bacteremic disease. Hib strains account for only 5%-10% of *H. influenzae* causing otitis media.

Several population-based studies of invasive Hib disease conducted within the last 10 years have provided estimates of the incidence of disease among children under 5 years of age, the major age group at risk. These studies have demonstrated attack rates of meningitis ranging from 51 cases per 100,000 children to 77/100,000 per year and attack rates of other invasive Hib disease varying from 24/100,000 to 75/100,000 per year (1). Thus, in the United States, approximately one of every 1,000 children under 5 years of age develops systemic Hib disease each year, and a child's cumulative risk of developing systemic Hib disease at some time during the first 5 years of life is about one in 200. Attack rates peak between 6 months and 1 year of age and decline thereafter. Approximately 35%-40% of Hib disease occurs among children 18 months of age or older, and 25% occurs above 24 months of age.

Incidence rates of Hib disease are increased in certain high-risk groups, such as Native Americans (both American Indians and Eskimos), blacks, individuals of lower socioeconomic status, and patients with asplenia, sickle cell disease, Hodgkin's disease, and antibody deficiency syndromes. Recent studies also have suggested that the risk of acquiring primary Hib disease for children under 5 years of age appears to be greater for those who attend day-care facilities than for those who do not (2,3).

The potential for person-to-person transmission of systemic Hib disease among susceptible individuals has been recognized in the past decade. Studies of secondary spread of Hib disease in household contacts of index patients have shown a substantially increased risk of disease among exposed household contacts under 4 years of age (4). In addition, numerous clusters of cases in day-care facilities have been reported, and recent studies suggest that secondary attack rates in day-care classroom contacts of a primary case also may be increased (5,6).

**HAEMOPHILUS b POLYSACCHARIDE VACCINE**

The Hib vaccine is composed of the purified, capsular polysaccharide of *H. influenzae* type b ([ $\alpha$ -3] ribose- $\beta$ 1  $\rightarrow$ 1 ribitol-1 phosphate-5 $\rightarrow$ ). Antibodies to this antigen correlate with protection against invasive disease. The Hib vaccine induces an antibody response that is directly related to the age of the recipient; infants respond infrequently and with less antibody than do older children or adults (7). Improved responses are observed by 18 months of age, although children 18-23 months of age do not respond as well as those 2 years of age or older. The frequency and magnitude of antibody responses reach adult levels at about 6 years of age (8,9). Levels of antibodies to the capsular polysaccharide also decline more rapidly in immunized infants and young children than in adults.

\*Official name: Haemophilus b Polysaccharide Vaccine.

In a manner similar to other polysaccharide antigens, revaccination with Hib vaccine results in a level of antibody comparable to that for a child of the same age receiving a first immunization (10). Such polysaccharide antigens have been termed "T-cell independent" because of their failure to induce the T-cell memory response characteristic of protein antigens.

Limited data are available on the response to Hib vaccine in high-risk groups with underlying disease. By analogy to pneumococcal vaccine, patients with sickle cell disease or asplenia are likely to exhibit an immune response to the Hib vaccine. Patients with malignancies associated with immunosuppression appear to respond less well. Additional data on the immune response to Hib vaccine in these groups are needed.

A precise protective level of antibody has not been established. However, based on evidence from passive protection in the infant rat model and from experience with agammaglobulinemic children, an antibody concentration of 0.15  $\mu\text{g/ml}$  correlates with protection (7,8,11). In the Finnish field trial, levels of capsular antibody greater than 1  $\mu\text{g/ml}$  in 3-week postimmunization sera correlated with clinical protection for a minimum of 1½ years (9,12,13). Approximately 75% of children 18-23 months of age tested achieved a level greater than 1  $\mu\text{g/ml}$ , as did 90% of 24-35 month old children (9). Measurement of Hib antibody levels is not routinely available, however, and determination of antibody levels following vaccination is not indicated in the usual clinical setting.

#### EFFECTIVENESS OF VACCINE

In 1974, a randomized, controlled trial of clinical efficacy was conducted in Finland among children 3-71 months of age (9). Approximately 98,000 children, half of whom received the Hib vaccine, were enrolled in the field trial and followed for a 4-year period for occurrence of Hib disease. Among children 18-71 months of age, 90% protective efficacy (95% confidence limits, 55%-98%) in prevention of all forms of invasive Hib disease was demonstrated for the 4-year follow-up period. Although no disease occurred among over 4,000 children 18-23 months of age immunized with Hib vaccine and followed for 4 years, only two cases occurred in the control vaccine recipients in this age group. As a result, vaccine efficacy in the subgroup of children immunized at 18-23 months of age could not be evaluated statistically. The vaccine was not efficacious in children under 18 months of age.

#### RE VaccINATION

Limited data regarding the potential need for revaccination are available at present. Current data show that children who have received the Hib vaccine 2-42 months previously have an immune response to the vaccine similar to that in previously unvaccinated children of the same age. No immunologic tolerance or impairment of immune response to a subsequent dose of vaccine occurs (10). As with other polysaccharide vaccines, the shorter persistence of serum antibodies in young children given Hib vaccine, compared with adults, suggests that a second dose of vaccine may be needed to maintain immunity throughout the period of risk, particularly for children in the youngest age group considered for vaccination (those 18-23 months of age). A second injection following the initial dose is likely to increase the protective benefit of vaccination for this high-risk group, because antibody titers 18 months after vaccination, although detectable in most vaccine recipients, are no longer significantly different from those in unvaccinated children of the same age.

#### RECOMMENDATIONS FOR VACCINE USE

Recently published data regarding vaccine efficacy and the risk of Hib disease among young children strongly support the use of Hib vaccine in the United States in high-risk persons for whom efficacy has been established. Specific recommendations are as follows:

1. Immunization of all children at 24 months of age is recommended. The precise duration of immunity conferred by a single dose of Hib vaccine at 24 months of age is not known, although, based on available data, protection is expected to last 1½-3½ years. Until further data are available to determine whether an additional dose of vaccine may be necessary to ensure long-lasting immunity, routine revaccination is not recommended.
2. Immunization of children at 18 months of age, particularly those in known high-risk groups, may be considered. Although the precise efficacy of the vaccine among children 18-23 months of age is not known, this age group accounts for approximately 12% of all invasive Hib disease among children under 5 years of age, and Hib vaccine has been shown by serologic methods to be immunogenic in most children of this age group. However, physicians and parents should be informed that the vaccine is not likely to be as effective in this age group as in older children. These younger children may need a second dose of vaccine within 18 months following the initial dose to ensure protection. Additional data regarding the duration of the antibody response are needed to define the timing of a second dose more precisely.

Children who attend day-care facilities are at particular risk of acquiring systemic Hib disease. Initial vaccination at 18 months of age for this high-risk group should be considered.

Children with chronic conditions known to be associated with increased risk for Hib disease should receive the vaccine, although only limited data on immunogenicity and clinical efficacy in this group are available. These conditions include anatomic or functional asplenia, such as sickle cell disease or splenectomy (14), and malignancies associated with immunosuppression (15).

3. Immunization of individuals over 24 months of age who have not yet received Hib vaccine should be based on risk of disease. The risk of invasive Hib disease decreases with increasing age over the age of 2 years. Because the vaccine is safe and effective, however, physicians may wish to immunize previously unvaccinated healthy children between 2 years and 5 years of age to prevent the Hib disease that does occur in this age group. The potential benefit of this strategy in terms of cases prevented declines with increasing age of the child at the time of vaccination. Therefore, children 2-3 years of age who attend day-care facilities should be given a higher priority than day-care attendees who are 4-5 years old.
4. Insufficient data are available on which to base a recommendation concerning use of the vaccine in older children and adults with the chronic conditions associated with an increased risk of Hib disease.
5. Vaccine is not recommended for children under 18 months of age.
6. Simultaneous administration of Hib and DTP vaccines at separate sites can be performed, because no impairment of the immune response to the individual antigens occurs under these circumstances.

#### SIDE EFFECTS AND ADVERSE REACTIONS

Polysaccharide vaccines are among the safest of all vaccine products. To date, over 60,000 doses of the Hib polysaccharide vaccine have been administered to infants and children, and several hundred doses have been given to adults (9,16). Only one serious systemic reaction has been reported thus far—a possible anaphylactic reaction that responded promptly to epinephrine. High fever (38.5 C [101.3 F] or higher) has been reported in fewer than 1% of Hib vaccine recipients. Mild local and febrile reactions were common, occurring in as many as half of vaccinated individuals in the Finnish trial. Such reactions appeared within 24 hours and rapidly subsided. Current preparations appear to result in fewer such local reactions. Simultaneous administration with DTP does not result in reaction rates above those expected with separate administration (17).

#### PRECAUTIONS AND CONTRAINDICATIONS

The Hib vaccine is unlikely to be of substantial benefit in preventing the occurrence of secondary cases, because children under 2 years old are at highest risk of secondary disease. Because the vaccine will not protect against nontypeable strains of *H. influenzae*, recurrent upper respiratory diseases, including otitis media and sinusitis, are not considered indications for vaccination.

#### NEW VACCINE DEVELOPMENT

New vaccines, such as the Hib polysaccharide-protein conjugate vaccines, are being developed and evaluated and may prove to be efficacious for children under 18 months of age.

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
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*Recommendations of the Immunization  
Practices Advisory Committee (ACIP)*

**Update: Prevention of *Haemophilus influenzae* Type b Disease**

*Haemophilus influenzae type b (Hib) is the most common cause of bacterial meningitis in the United States. It also causes other serious invasive illnesses, including epiglottitis, sepsis, cellulitis, septic arthritis, osteomyelitis, pericarditis, and pneumonia. By 5 years of age, one of every 200 children in the United States will have had a systemic infection due to Hib. A polysaccharide vaccine against systemic Hib disease was licensed in the United States in April 1985. Information on the vaccine and Immunization Practices Advisory Committee (ACIP) guidelines for its use should be consulted (1). The purpose of this statement is to update these recommendations and to provide guidelines for the prevention of secondary cases of Hib disease.*

**CHEMOPROPHYLAXIS**

**Risk of Secondary Disease.** Secondary disease, defined as illness within 1-60 days following contact with a child who has Hib disease, accounts for less than 5% of all invasive Hib disease. However, six studies of household contacts of Hib patients found a secondary attack rate of 0.3% in the month following disease onset in the index patient, which is about 600-fold higher than the age-adjusted risk in the general population (2-7). Among these studies, the attack rate among household contacts varied markedly with age: 4% for children under 2 years of age; 2% for children 2-3 years of age; 0.1% for children 4-5 years of age; and 0% for those over 6 years of age (2-7). Among these household contacts, 64% of secondary cases occurred within the first week (excluding the first 24 hours) of disease onset in the index patient; 20%, during the second week; and 16%, during the third and fourth weeks.

The risk of secondary disease among children who were exposed to a primary case in day-care and who did not receive rifampin prophylaxis has been examined in four studies. A national collaborative study that calculated secondary attack rates for household and day-care classroom contacts found that one (1%) of 91 children under 4 years of age in day-care acquired disease in the month following the index patient, compared with three (2%) of 125 household contacts under 4 years of age (2). A multicenter study in Seattle-King County, Washington; Oklahoma; and Atlanta, Georgia, found that the risk of secondary Hib disease among day-care classroom contacts was age-dependent; 10 (3%) cases occurred among the 376 contacts 0-23 months old, whereas none of the 379 classroom contacts older than 23 months of age acquired secondary disease (8). No cases occurred among children who attended day-care for fewer than 25 hours per week. In this study, classroom contacts were defined as children who spent more than half their day-care time in the same classroom as a child with primary Hib disease in the week before disease onset of the primary case. The overall risk for classroom contacts was 0.7% (10/1,388), 20 times higher than the risk for other children in the center (0.04% [2/5,639]). Thirty-three percent of the secondary cases occurred within 3 weeks of onset of the index case; 13%, between days 21 and 40; and 53%, between days 41 and 60. Meningitis and other systemic Hib infections were equally likely to result in secondary cases.

Two prospective studies have examined the risk of subsequent Hib disease in day-care facilities. In Dallas County, Texas, follow-up for 60 days of classroom contacts revealed no cases of secondary disease in 361 children under 2 years old, and a secondary attack rate of 0.5% (1/213) in those 2-3 years of age (9). Other cases of Hib disease occurred but could not be classified as secondary cases because these children enrolled in the day-care facility after the index patient became ill. Since it is known that rates of asymptomatic transmission are elevated in day-care classrooms with children with Hib disease, some of these cases may have been associated with the index case.

A similar surveillance study was conducted in Minnesota. No cases of secondary Hib disease were found among 370 day-care contacts under 2 years of age; 263 (71%) were classroom contacts. These were defined as children who spent more than 8 hours in the same classroom as the primary case in the week before the patient with primary disease became ill. Similarly, secondary cases were not seen in 716 children 2-3 years of age, of whom 421 (59%) were classroom contacts (10).

The disparities in the risk of day-care-associated secondary Hib disease in Minnesota; Dallas County, Texas; and the two multicenter studies remain unexplained. Possible reasons include differences among the several study areas in day-care characteristics, such as classroom size and age distribution of children, which might affect intensity and duration of contact. There may be further unrecognized differences in epidemiologic factors or invasiveness of prevalent Hib strains.

**Efficacy of Rifampin Prophylaxis.** Most children at risk of secondary disease are too young to respond to the Hib polysaccharide vaccine. Therefore, the main preventive measure presently available is rifampin administration. Currently available data from several studies indicate rifampin in a dosage of 20 mg/kg per dose once daily (maximum daily dose 600 mg) for 4 days eradicated Hib carriage in 95% or more of contacts of primary cases, including children in day-care facilities (17-19). In a randomized placebo controlled trial, rifampin in the currently recommended dosage administered to all household and day-care classroom contacts, including adults, significantly decreased secondary Hib disease among household and day-care contacts (none of 303 rifampin-treated contacts under 4 years of age had secondary disease, compared with four of 216 placebo-treated contacts under 4 years of age [ $p = 0.03$ ] (2); the number of cases was insufficient to evaluate efficacy in the household or day-care setting alone. However, the collaborative study of day-care centers cited above found that among classroom contacts of Hib patients, children aged 0-23 months who received rifampin prophylaxis were significantly less likely to develop secondary disease than children who did not take rifampin (none of 232, compared with 10 [3%] of 376 [ $p < 0.02$ ] (8). Secondary disease did not develop in day-care classes in which over 75% of the class received rifampin. However, rifampin prophylaxis is unlikely to be 100% effective, and a day-care center in which rifampin prophylaxis failed to prevent subsequent disease has been reported (14).

**Implementation of Chemoprophylaxis.** Rifampin is available in 150-mg and 300-mg capsules. For those unable to swallow capsules, rifampin may be mixed with several teaspoons of applesauce immediately before administration, resulting in acceptable serum and salivary levels (15). Although there has been more experience with the applesauce mixture, a suspension of rifampin may also be freshly prepared in United States Pharmacopeia syrup; the preparation should be vigorously shaken before use. Side effects of rifampin in the recommended dose include nausea, vomiting, diarrhea, headache, or dizziness, which occurred among 20% of those taking rifampin and 11% of placebo recipients. No serious reactions occurred (2). Those taking rifampin (including parents and day-care staff) should be informed that orange discoloration of urine, discoloration of soft contact lenses, and decreased effectiveness of oral contraceptives can occur.

In implementing chemoprophylaxis in day-care centers, it is important to ensure that all classroom contacts receive rifampin during the same period. Some local and state health departments have facilitated the timely implementation of chemoprophylaxis by coordinating rifampin administration following consultation with private physicians or by providing information to parents of day-care contacts.

#### VACCINE

**Effect of Haemophilus b Polysaccharide Vaccine on Nasopharyngeal Carriage.** Limited data are available on the effect of the Haemophilus b polysaccharide vaccine on nasopharyngeal carriage of the organism. By analogy to carriage studies after serogroups A and C meningococcal polysaccharide vaccination, some reduction in acquisition of carriage may occur shortly after immunization, but no long-term effect has been noted (16-18).

**Use of Haemophilus b Polysaccharide Vaccine in Children with Preceding Hib Disease.** Studies have shown that the development of anticapsular antibodies following invasive Hib disease is largely age-dependent. A study of acute and convalescent sera from 125 patients with meningitis, septicemia, or epiglottitis due to Hib determined that, among those who acquired disease when they were younger than 18 months, 41 (85%) of 48 failed to develop an adequate antibody response, in contrast to 18 (23%) of 77 of those older than 18 months (19). Cases have been reported in which children who do not mount an antibody response after an invasive episode of Hib have developed a second systemic infection with the organism (20).

#### RECOMMENDATIONS

The primary strategy for preventing Hib disease is immunization. Children should be vaccinated at 24 months of age. Those at high risk for Hib disease, including children attending day-care, may be given the vaccine at 18 months of age. ACIP guidelines for use of the vaccine should be consulted (7). This update addresses chemoprophylaxis (recommendations 1-7) and additional vaccine issues (recommendations 8 and 9).

**Chemoprophylaxis.** Although unexplained disparities in available data prevent a precise estimate of the magnitude of risk among day-care contacts, it is likely that the increased risk of disease observed among young household contacts is also present among day-care classroom contacts under 2 years of age. Since rifampin prophylaxis is effective in preventing subsequent cases in this high-risk group, the ACIP recommends that:

1. Contacts of all ages who develop symptoms suggestive of invasive Hib disease, such as fever or headache, be evaluated promptly by a physician.
2. In any household in which a case of invasive Hib disease has occurred and in which another child under 4 years of age resides, all members of the household, including adults, should receive rifampin according to the following regimen: rifampin in a dosage of 20 mg/kg per dose once daily (maximal daily dose 600 mg) for 4 days; the dose for neonates (under 1 month of age) is 10 mg/kg once daily for 4 days.
3. In day-care classrooms in which a case of Hib disease has occurred and in which another child under 2 years of age has been exposed, all parents should be notified (preferably in writing) regarding the occur-

- rence of the case and the possibility of increased risk to their children. They should be informed about the symptoms and the need for prompt medical evaluation if symptoms occur. They should also be notified of the availability of rifampin prophylaxis. Although the data on which to base recommendations are not optimal, and some authorities disagree, the consensus of the ACIP is as follows: In a day-care classroom in which a case of systemic Hib disease has occurred, and in which one or more children under 2 years old have been exposed, strong consideration should be given to administering rifampin prophylaxis to all children and staff in the classroom, regardless of age.
- Rifampin should not be used in pregnant women, as its effect on the fetus has not been established, and it is teratogenic in laboratory animals.
  - Chemoprophylaxis should be instituted as rapidly as possible. If more than 14 days have passed since the last contact with the index patient, the benefit of chemoprophylaxis is likely to be decreased.
  - All children convalescing from systemic Hib disease who are anticipated to resume close contact with other young children, at home or in day-care, should receive rifampin immediately after completing treatment for their illness. Therapy for systemic disease does not reliably eradicate respiratory carriage of Hib, and some physicians may wish to give rifampin to all index patients.
  - In day-care classrooms in which children are to receive chemoprophylaxis, children who have received the Haemophilus b polysaccharide vaccine should also receive rifampin. Although these children are felt to be at decreased risk for disease, the vaccine probably does not affect carriage of the organism, which they may pass on to susceptible classmates.
  - Children who have had invasive Hib disease when they were under 24 months of age should still receive the vaccine according to previous recommendations, since most children under 24 months of age fail to mount an immune response to the clinical disease.
  - Satisfactory response to the vaccine is not consistent among children 18-23 months of age, and most authorities believe that these children should be revaccinated. Although data on the precise timing of this second dose are not currently available, it would be reasonable to reimmunize 2-12 months after the initial dose but not before 24 months of age. Previous immunization does not change the immune response or adverse reaction to a subsequent dose of the vaccine [21].

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Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Update: Prevention of *Haemophilus influenzae* Type b Disease**

On June 23, 1987, the Immunization Practices Advisory Committee (ACIP) reviewed preliminary postmarketing surveillance data presented at an April 20, 1987, FDA workshop on *Haemophilus influenzae* type b (Hib) polysaccharide vaccines (see article below). These data were evaluated in light of the current ACIP recommendations for use of the vaccine (1) and for prophylaxis with rifampin (2) in the prevention of invasive Hib disease.

The ACIP believes that the preliminary data from these ongoing studies do not indicate a need for changes in the present recommendations for vaccine use. It should be emphasized that vaccination is not a substitute for prophylaxis with rifampin in children exposed to Hib disease.

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Current Trends

**FDA Workshop on *Haemophilus* b Polysaccharide Vaccine –  
A Preliminary Report**

In April 1985, the Food and Drug Administration (FDA) licensed the first *Haemophilus* b polysaccharide vaccine. Two additional companies were licensed to produce similar vaccines at the end of 1985. Estimation of the efficacy of the vaccines was based on the results of a randomized, controlled clinical trial conducted in Finland. In that trial, which was conducted among children 18-71 months of age, efficacy was estimated to be 90%, with few serious adverse reactions reported (1). In addition, each manufacturer performed safety and immunogenicity studies before licensure. Upon licensure, FDA asked each company to conduct postmarketing studies for rare adverse events in larger populations.

After licensure, FDA, CDC, the manufacturers, and individual investigators received spontaneous reports of invasive *Haemophilus influenzae* type b (Hib) disease in previously vaccinated children. One investigator published data suggesting that vaccine failure might be due to an inability to induce an appropriate antibody response (2). Several groups of investigators initiated studies to further evaluate the vaccine's efficacy. Investigators from Northern California Kaiser Permanente Health Plan and the Minnesota Department of Health reported observing some cases of invasive Hib disease during the 1-week period immediately following vaccination.

These observations prompted FDA to hold a workshop on April 20, 1987, to discuss the ongoing studies of the vaccine's efficacy. It was recognized that these studies

were incomplete at the time of the meeting. The workshop was an open meeting involving experts in *Haemophilus* disease, epidemiology, and statistics. Two issues were addressed: the efficacy of the vaccine and the interpretation of reports of invasive Hib disease in the 7 days following vaccination.

Investigators from the Northern California Kaiser Permanente Health Plan, Yale University and the University of Texas, the Minnesota Department of Health, and CDC presented data. Each of these groups had been conducting studies for 2 years. Because of the normal delay in antibody formation following vaccination, the investigators had considered children to be vaccinated only if they had received vaccine 21 days or more (14 days or more in the CDC study) before the onset of disease. A brief synopsis of the data follows.

The Kaiser group presented data from a prospective cohort study and a case-control study. The former was not randomized and included about 122,000 children between 18 months and 5 years of age. There were 24 cases of invasive Hib disease in the unvaccinated group and two cases in the vaccinated group. The point estimate of the vaccine's efficacy was 89% (95% confidence interval [CI], 52 to 97). A case-control study from this cohort yielded a point estimate of 81% (95% CI, 10 to 96). Four children in this population developed disease within 7 days after vaccination. One of the patients had been immunized specifically because of exposure to Hib.

Yale University and the University of Texas conducted a joint birth-certificate-matched case-control study among children 24 to 59 months of age. Investigators identified 17 cases in Connecticut and 25 in Dallas. Twenty-four percent of the patients and 50% of the controls in Connecticut were vaccinated; in Dallas, 11% of the patients and 32% of the controls were vaccinated. The point estimate of efficacy in Connecticut and Dallas was 89% (95% CI, 69 to 97). In this study, one patient had been vaccinated within 7 days of the date of onset, and one control had been vaccinated within 7 days of the reference date, indicating no increased risk of Hib disease.

The Minnesota Department of Health conducted a birth-certificate-matched case-control study among children 24 to 59 months of age. From September 1985 to March 1987, investigators identified 53 cases. Eight of the patients were excluded because of pre-existing risks for Hib disease.\* Fifteen (33%) of the 45 remaining patients were vaccinated, compared with 22 (24%) of the 90 controls. The estimated protective efficacy was -86% (95% CI, -415 to 33). The Minnesota investigators observed three cases of invasive Hib disease within 7 days of vaccination.

CDC conducted a multistate day-care-based case-control study among children 18 to 59 months of age. There were 108 patients and 251 controls. Nineteen percent of the patients and 29% of the controls had been vaccinated. The point estimate of efficacy was 44% (95% CI, -5 to 70). Investigators identified four patients with onsets of invasive Hib disease during the first week after vaccination; five controls had been vaccinated during a comparable interval.

Unlike these relatively small observational studies, the clinical trial of vaccine efficacy in Finland was a large, prospective, randomized trial involving over 48,000 recipients of *Haemophilus* b polysaccharide vaccine. This study is considered important because of its design and size. With the exception of the Minnesota study, all the efficacy studies presented at the April 20, 1987, workshop produced results that are not inconsistent with the results of the Finnish trial. However, since the more recent studies were observational, they may be subject to biases not usually found in randomized, controlled trials. These studies are continuing, and the data will be reassessed in the near future.

\*Including immunodeficiency, sickle cell anemia, or a previous episode of Hib disease.

Although the Finnish study did not identify any cases of Hib disease within 7 days of vaccination, further information is necessary to evaluate the meaning of cases found soon after vaccination in the more recent studies. In any event, physicians should be aware that cases may occur in the week after vaccination, prior to onset of the protective effects of the vaccine.

While further analysis of these data is in progress, it was concluded that, based on evaluation of these preliminary data, the benefits of the vaccine continue to outweigh any potential risk. Therefore, physicians are urged to vaccinate their patients according to present ACIP recommendations.

Any adverse events, including vaccine failure, should be reported either to the manufacturer or to FDA.

*Reported by: Div of Bacterial Products, Div of Epidemiology and Biostatistics, Center for Drugs and Biologics, Food and Drug Administration.*

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Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Update: Prevention of *Haemophilus influenzae* Type b Disease**

Haemophilus b Conjugate Vaccine (Diphtheria Toxoid-Conjugate) has recently been licensed for use in children 18 months of age or older for the prevention of *Haemophilus influenzae* type b (Haemophilus b) disease. This vaccine consists of Haemophilus b capsular polysaccharide covalently linked to diphtheria toxoid (conjugate vaccine).

A previously developed vaccine consisting of the Haemophilus b capsular polysaccharide alone (polysaccharide vaccine) was shown to be effective in Finnish children over 24 months of age (1), the age group in which approximately 20% of all invasive Haemophilus b infections among U.S. children less than 5 years of age can be expected to occur (2). A similar, but not identical, polysaccharide vaccine was licensed for use in the United States in April 1985 on the basis of data demonstrating biochemical characteristics and immunogenicity comparable to the vaccine used in the original Finnish trial (3). In that Finnish trial, polysaccharide vaccine was not effective in children less than 18 months of age. Because of the small sample size, efficacy could not be demonstrated in children 18 to 23 months of age. Polysaccharide vaccine was immunogenic (as measured by antibody production) in children 18 to 23 months old, but less so than it was in older children (1).

Conjugate vaccine was developed with the ultimate goal of providing an effective vaccine for infants and younger children. Preliminary data from a new Finnish study suggest that conjugate vaccine was 87% effective in preventing Haemophilus b disease when administered in a three-dose regimen to infants 3 to 6 months of age (4). However, licensure of conjugate vaccine for use in infants in the United States cannot be considered until this and other efficacy trials are further evaluated. Since antibody production after vaccination with conjugate vaccine in children 18 months of age or older is substantially greater than that after vaccination with polysaccharide vaccine, conjugate vaccine has been licensed for use in these children.

**Safety**

When conjugate vaccine alone was given to over 1,000 adults and children, no serious adverse reactions were observed (5-12). When conjugate vaccine was given with diphtheria and tetanus toxoid and pertussis vaccine (DTP) and inactivated polio vaccine (IPV) to 30,000 infants, the rate and extent of serious adverse reactions did not differ from those seen when DTP was administered alone (4). In one study of over 500 children 15 to 24 months of age, no significant difference in local or systemic side effects occurred between groups of children vaccinated with either polysaccharide vaccine or conjugate vaccine (7). Local reactions were noted for 10.3% of children receiving polysaccharide vaccine and 12.5% of children receiving conjugate vaccine, while moderate fever (temperature >39.0 °C [ $>102.2$  °F]) occurred in 1.4% of children vaccinated with polysaccharide vaccine and 0.7% of children vaccinated with conjugate vaccine.

**Immunogenicity**

In several studies using different regimens of vaccine administration, conjugate vaccine has shown greater immunogenicity than polysaccharide vaccine (5-9,11,12). Response to a single dose of either polysaccharide vaccine or conjugate vaccine in children 15 to 24 months of age was specifically addressed in a randomized, double-blind study recently completed in the United States (7). More than 90% of children vaccinated with conjugate vaccine responded with antibody levels considered to be protective (0.15 µg/mL), whereas less than 50% of children vaccinated with polysaccharide vaccine had such a response. Over 60% of children vaccinated with conjugate vaccine, but less than 30% of those vaccinated with polysaccharide vaccine, produced levels of antibody considered to be indicative of

## IMPORTANT INFORMATION ABOUT HAEMOPHILUS INFLUENZAE TYPE b DISEASE AND HAEMOPHILUS b POLYSACCHARIDE VACCINE

*Please read this carefully*

HAEMOPHILUS b  
5/1/86

**WHAT IS HAEMOPHILUS INFLUENZAE TYPE b DISEASE?** *Haemophilus influenzae* type b (Haemophilus b) is a bacterium which can cause severe disease, especially in children less than 5 years of age. This bacterium does not cause the "flu" (influenza). In the United States, Haemophilus b causes about 12,000 cases of meningitis (infection of the covering of the brain) each year, mostly in children under 5 years of age. About 1 child in every 20 with meningitis caused by Haemophilus b dies of it and about 1 out of 4 has permanent brain damage. Haemophilus b can also cause pneumonia and infections of other body systems such as blood, joints, bone, soft tissue, throat, and the covering of the heart.

About 1 in every 200 children in the United States will have a moderate to severe disease caused by Haemophilus b before their fifth birthday. Severe Haemophilus b disease is most common in children between 6 months and 1 year of age, but almost 40 percent of severe disease occurs in children 18 months of age or older.

### HAEMOPHILUS b POLYSACCHARIDE VACCINE:

The Haemophilus b polysaccharide vaccine (Haemophilus b vaccine) is given by injection. Nearly 90 percent of children 24 months of age or older who receive the vaccine are protected for at least 1½ years against the severe diseases caused

by Haemophilus b bacteria. Whether the vaccine provides protection against ear infections caused by Haemophilus b bacteria is not known. It does not protect against ear infections caused by other types of Haemophilus. The vaccine does not protect against meningitis caused by other bacteria. The vaccine will not cause Haemophilus disease.

### WHO SHOULD RECEIVE THE HAEMOPHILUS b VACCINE?

1. All children 2 years of age should be immunized—Nearly 90 percent of children who are immunized when 2 years of age or older are protected against the severe forms of the disease. Ideally, children should be immunized within 1 month following their second birthday. Protection lasts for a minimum of 1½ years.
2. Children 1½ to 2 years of age may be considered for immunization if they are in a high risk group, such as those attending day-care facilities—The vaccine may not be as effective in children 1½ to 2 years of age as in children 2 years of age or older, and, therefore, it is not recommended routinely for this age group. However, because children who attend day-care facilities are more likely to develop severe Haemophilus b disease than those who do not, day-care attendees in this age group may be immunized. Children who were under 24 months of age when

*(PLEASE READ OTHER SIDE)*

Forms provided by: Montana Immunization Program  
Dept. of Health & Environmental Sciences  
Helena, MT 59620

they received a dose of Haemophilus b vaccine should receive a second dose 2-12 months after the initial dose but not before 24 months of age.

3. Children 3 and 4 years of age may be considered for immunization if they attend a day-care facility—Fewer cases of severe disease occur in children over the age of 2 years. However, children attending day-care facilities, especially those 3 years of age, may benefit from the vaccine.
4. No children younger than 1½ years of age should be immunized—Children younger than 1½ years of age are not protected by the Haemophilus b vaccine.
5. Schoolchildren and adults usually should not be immunized.

**POSSIBLE SIDE EFFECTS FROM THE VACCINE:**

Polysaccharide vaccines such as Haemophilus b vaccine are considered relatively free of side effects. In studies with an early Haemophilus b vaccine, redness and/or swelling occurred in 5 to 51 percent of those who received the vaccine, and a fever of 101°F or higher at 24 hours after vaccination occurred in up to 13 percent. Recent information from one manufacturer about the vaccine now available in the United States indicates that approximately 1 out of every 67 children who receive the current vaccine will get redness and/or swelling in the area where the shot was given. About 1 out of

every 100 children will have a fever of 101.3°F or higher. These reactions begin within 24 hours after the shot is given, but generally go away quickly. With any vaccine or drug, there is a rare possibility that allergic or other reactions, such as febrile seizures or even death, could occur.

**WARNING—SOME PERSONS SHOULD NOT TAKE THIS VACCINE WITHOUT CHECKING WITH A DOCTOR:**

- Anyone who is sick right now with something more serious than a cold.
- Anyone who has had a serious reaction to a product containing thimerosal, a mercurial antiseptic.

**QUESTIONS:** If you have any questions about Haemophilus b disease or Haemophilus b vaccine, please ask now or call your doctor or health department before you sign this form.

**REACTIONS:** If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic during the 4 weeks after receiving the vaccine, please report it to:

**PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS**

*I have read the information on this form about Haemophilus b disease and Haemophilus b vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of the Haemophilus b vaccine and request that it be given to the person named below for whom I am authorized to make this request.*

HAEMOPHILUS b  
5/1/86

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                       |            |       |           |      |
|--|------------|-------|-----------|------|
| Last Name  | First Name | MI    | Birthdate | Age  |
| Address  |            |       |           |      |
| City   | County     | State | Zip       |      |
| X  |            |       |           |      |
| Signature of person to receive vaccine or person authorized to make the request. |            |       |           | Date |

| FOR CLINIC USE     |
|--------------------|
| Clinic Ident.      |
| Date Vaccinated    |
| Manuf. and Lot No. |
| Site of injection  |

**FOR DATA PROCESSING USE ONLY (OPTIONAL)**

|   |   |   |   |   |
|---|---|---|---|---|
| VACCINE HISTORY: PLACE CHECK <input type="checkbox"/> |   | IN BOX IF HISTORY PREVIOUSLY SUBMITTED  |   |   |
| DTP:  | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> |
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|   |   |   | RUBELLA:                                | HAEMOPHILUS b:                          |
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|   |   |   |   | <u>    </u> / <u>    </u> / <u>    </u> |

long-term protection (1.0  $\mu\text{g/mL}$ ).<sup>\*</sup> Children given conjugate vaccine at 15 to 24 months of age had significantly higher levels of antibody to Haemophilus b polysaccharide 1 year after vaccination than did children receiving polysaccharide vaccine (8). Conjugate vaccine recipients responded to a booster dose of either polysaccharide vaccine or conjugate vaccine with higher geometric mean antibody levels than did those initially vaccinated with polysaccharide vaccine (8).

In another study, children with sickle cell syndromes who received conjugate vaccine had higher postvaccination levels of antibody to Haemophilus b polysaccharide than did similar children given polysaccharide vaccine (13). The studies to date showing increased immunogenicity in children less than 18 months of age (5,6,9,11) suggest that conjugate vaccine may be functioning as a T-cell dependent antigen. This finding contrasts with the lack of immunogenicity in infants and the absence of immunologic memory characteristic of T-cell independent polysaccharide vaccines.

#### Biological Activity

Several investigators have demonstrated that conjugate vaccine produces functional activity against Haemophilus b similar to that produced by polysaccharide vaccine. In one randomized, double-blind study, adults vaccinated with conjugate vaccine had serum bactericidal titers for Haemophilus b at least as high as those of adults receiving polysaccharide vaccine (12). In addition, sera from adults vaccinated with conjugate vaccine were protective in an infant rat model of Haemophilus b disease, whereas similarly diluted sera from persons receiving polysaccharide vaccine showed no protective activity. In a separate study, sera from 9- to 14-month-old children given conjugate vaccine showed greater opsonic activity against Haemophilus b organisms than did sera from children vaccinated with polysaccharide vaccine (14). Both studies showed a correlation between functional activity and serum levels of antibody to Haemophilus b polysaccharide and suggest that antibody produced in response to conjugate vaccine is biologically equivalent to that produced in response to polysaccharide vaccine.

#### Immunization Practices Advisory Committee (ACIP) Recommendations

1. The ACIP recommends that all children receive conjugate vaccine at 18 months of age. The efficacy of conjugate vaccine in children 18 months of age or older has not been determined in field trials. However, studies comparing antibody production in children receiving conjugate vaccine with that in children receiving polysaccharide vaccine suggest that conjugate vaccine is likely to be more effective than polysaccharide vaccine. The ACIP therefore recommends use of conjugate vaccine in all children vaccinated against Haemophilus b disease.
2. While the duration of immunity after a single dose of conjugate vaccine is unknown at this time, it is expected to be at least 1.5 to 3 years. Until further information is available, revaccination is not recommended for children receiving conjugate vaccine at 18 months of age or older.
3. Vaccination of children more than 24 months of age who have not yet received Haemophilus b vaccine should be based on risk of disease. Children considered at high risk for Haemophilus b disease, including those attending day-care centers, those with anatomic or functional asplenia (i.e., sickle cell disease or splenectomy), and those with malignancies associated with immunosuppression, should receive the vaccine. Although risk of disease decreases with increasing age, physicians may wish to vaccinate previously healthy children between 2 and 5 years of age to prevent disease that can occur in this group.
4. Because many children who received polysaccharide vaccine between the ages of 18 and 23 months may have had a less than adequate response to the vaccine, they should be revaccinated with a single dose of conjugate vaccine. Revaccination should take place a minimum of 2 months after the initial dose of polysaccharide vaccine.
5. There is no need to routinely revaccinate children who received polysaccharide vaccine at 24 months of age or older.
6. Children who had invasive Haemophilus b disease when they were less than 24 months of age should still receive vaccine according to the above recommendations since most children less than 24 months of age fail to develop adequate immunity following natural infection (15).

<sup>\*</sup>It should be noted that three of four lots of polysaccharide vaccine used in this study had been heat-sized, a process which may reduce immunogenicity. However, children receiving non-heat-sized polysaccharide vaccine also had postimmunization levels of antibodies to Haemophilus b polysaccharide that were lower than those observed in children vaccinated with conjugate vaccine. In another study in which vaccine recipients were tested at 1 month and again at 1 year after completion of the immunization series, 9- to 15-month-old children who had received two doses of conjugate vaccine had significantly higher titers of antibody to Haemophilus b polysaccharide than did similar children who had received two doses of non-heat-sized polysaccharide vaccine (5).

7. Although increases in serum diphtheria anti-toxin levels can follow administration of conjugate vaccine, this vaccine should not be considered an immunizing agent against diphtheria. No changes in the schedule for administration of diphtheria toxoid, customarily given as DTP, should be made secondary to the use of conjugate vaccine.
8. Vaccination with either polysaccharide vaccine or conjugate vaccine probably does not inhibit asymptomatic carriage of *Haemophilus b* organisms. Although vaccinated children may be protected from invasive disease, they may pass the organism on to susceptible children. In addition, no vaccine is 100% effective. Therefore, chemoprophylaxis of household or day-care contacts of children with *Haemophilus b* disease should be directed at vaccinated as well as unvaccinated contacts. Because of the length of time necessary to generate an immunologic response to the vaccines, vaccination does not play a major role in the management of patients with *Haemophilus b* disease or their contacts. Vaccine may be given to previously unvaccinated children of appropriate age to provide protection against future exposure.
9. Conjugate vaccine and DTP may be given simultaneously at different sites. Data are lacking on concomitant administration of conjugate vaccine and measles-mumps-rubella (MMR) or oral polio (OPV) vaccines. However, if the recipient is unlikely to return for further vaccination, simultaneous administration of all vaccines appropriate to the recipient's age and previous vaccination status is recommended (including DTP, OPV, MMR, and conjugate vaccine).

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**IMPORTANT INFORMATION ABOUT  
HAEMOPHILUS INFLUENZAE TYPE b DISEASE  
AND  
HAEMOPHILUS b CONJUGATE VACCINE**

*Please read this carefully*

**HAEMOPHILUS b  
Conjugate 6/1/89**

**WHAT IS HAEMOPHILUS INFLUENZAE TYPE b DISEASE?**

*Haemophilus influenzae* type b (Haemophilus b) is a bacterium which can cause serious disease, especially in children under 5 years of age. This bacterium does not cause the "flu" (influenza). In the United States, Haemophilus b causes about 12,000 cases of meningitis (infection of the covering of the brain) each year, mostly in children under 5 years of age. About 1 child in every 20 with meningitis caused by Haemophilus b dies of it and about 1 out of 4 has permanent brain damage. Haemophilus b can also cause pneumonia and infections of other body systems such as blood, joints, bone, soft tissue, throat, and the covering of the heart.

About 1 in every 200 children in the United States will have a moderate to severe disease caused by Haemophilus b before their fifth birthday. Serious Haemophilus b disease is most common in children between 6 months and 1 year of age, but 30 to 40 percent of severe disease occurs in children 18 months of age or older.

**HAEMOPHILUS b CONJUGATE VACCINE:**

There are at least two types of licensed Haemophilus b conjugate vaccines available for use. Diphtheria toxoid

or an altered, inactive diphtheria toxin is a part of the vaccine.

The Haemophilus b conjugate vaccine is given by injection. More than 90 percent of 18-to 24-month-old children given this vaccine responded by making substances in their blood (antibodies) that are considered to provide protection for at least 1 year against the severe diseases caused by Haemophilus b bacteria. However, several days are required for any protection to be obtained after immunization. Whether the vaccine provides protection against ear infections caused by Haemophilus b bacteria is not known. It does not protect against disease caused by other types of Haemophilus. The vaccine does not protect against meningitis caused by other bacteria. The vaccine is not known to cause Haemophilus disease.

The Haemophilus b conjugate vaccine first became available in 1988 and its use is preferred over an earlier type of vaccine called the Haemophilus b polysaccharide vaccine, which first became available in 1985.

**WHO SHOULD RECEIVE THE HAEMOPHILUS b CONJUGATE VACCINE?**

1. A single dose of the vaccine is recommended for all children at 18 months of age. Children 18 months to 23 months of age should also receive a dose if they have not already been immunized.

(PLEASE READ OTHER SIDE)

- Children 24 to 60 months of age may be considered for immunization, especially if they are believed to be at high risk for getting *Haemophilus b* disease. This includes children attending day-care facilities and children with certain medical conditions such as sickle cell disease, those whose spleens have been surgically removed, and children with cancers associated with decreased ability to fight infections.
- Children under 18 months of age should not be immunized, because the vaccine is not approved for use in children younger than 18 months of age.
- Children 60 months of age and older and adults normally would not be immunized.
- A second dose (booster dose) of vaccine is not recommended at this time.
- Children who received the other type of *Haemophilus b* vaccine (called the *Haemophilus b* polysaccharide vaccine) between the ages of 18 and 23 months should also receive the conjugate vaccine. Children who received the polysaccharide vaccine at 24 months of age or older do not need to receive the conjugate vaccine, but there is no known increased risk from the vaccine if they are reimmunized.

#### POSSIBLE SIDE EFFECTS FROM THE VACCINE:

The *Haemophilus b* conjugate vaccine has few side effects. Information about the vaccines now available in the United States indicates that approximately 1 out of every 8 children who receive the vaccine will get some redness, swelling, or tenderness in the area where the shot was given. About 1 out of every 140 children will have a fever of 102.2°F. or higher. These reactions begin

within 24 hours after the shot is given, but generally go away by 48 hours after immunization. Other possible reactions such as vomiting, diarrhea, or crying may occur in approximately 1 out of every 100 children. With any vaccine or drug, there is a rare possibility that allergic or other reactions, such as febrile seizures or even death, could occur.

#### WARNING—SOME PERSONS SHOULD NOT TAKE THIS VACCINE WITHOUT CHECKING WITH A DOCTOR:

- Anyone who is sick right now with something more serious than a cold.
- Anyone who has had a serious reaction to a product containing thimerosal, a mercurial antiseptic (included in one of the vaccines that is in use).
- Anyone who had an allergic reaction to a vaccine containing diphtheria toxoid vaccine so serious that it required medical treatment.

#### QUESTIONS:

If you have any questions about *Haemophilus b* disease or *Haemophilus b* conjugate vaccine, please ask now or call your doctor or health department before you sign this form.

#### REACTIONS:

If the person who received the conjugate vaccine has a convulsion or other serious reaction, the person should be seen promptly by a doctor.

If the person who received the conjugate vaccine gets sick and visits a doctor, hospital, or clinic during the 4 weeks after immunization, please report it to:

#### PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

*I have read or have had explained to me the information on this form about Haemophilus b conjugate vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of the haemophilus b conjugate vaccine and request that it be given to me or to the person named below for whom I am authorized to make this request.*

*Haemophilus b  
Conjugate 6/1/89*

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                       |       |       |            |      | FOR CLINIC USE         |  |
|--|-------|-------|------------|------|------------------------|--|
| Name: Last   | First | MI    | Birthdate: | Age: | Clinic Identification: |  |
| Address: Street  |       |       | County:    |      | Date Vaccinated:       |  |
| City   |       | State | Zip        |      | Manuf. and Lot No.:    |  |
| Signature of person to receive vaccine or person authorized to make the request: |       |       |            |      | Site of Injection:     |  |
| X _____ Date: _____  |       |       |            |      |                        |  |

FOR DATA PROCESSING USE ONLY (OPTIONAL)

| VACCINE HISTORY   |   |    |   |                  |    |   |        |                  |   |          |    |   |   |    |   |   |    |
|---|---|----|---|------------------|----|---|--------|------------------|---|----------|----|---|---|----|---|---|----|
| <input type="checkbox"/> (Place check in box if history previously submitted) |   |    |   |                  |    |   |        |                  |   |          |    |   |   |    |   |   |    |
| DTP:  |   |    |   | HAEMOPHILUS bPV: |    |   |        | HAEMOPHILUS bCV: |   |          |    |   |   |    |   |   |    |
| m   | d | yr | m | d                | yr | m | d      | yr               | m | d        | yr | m | d | yr | m | d | yr |
| POLIO:  |   |    |   | MEASLES:         |    |   | MUMPS: |                  |   | RUBELLA: |    |   |   |    |   |   |    |
| m   | d | yr | m | d                | yr | m | d      | yr               | m | d        | yr | m | d | yr | m | d | yr |

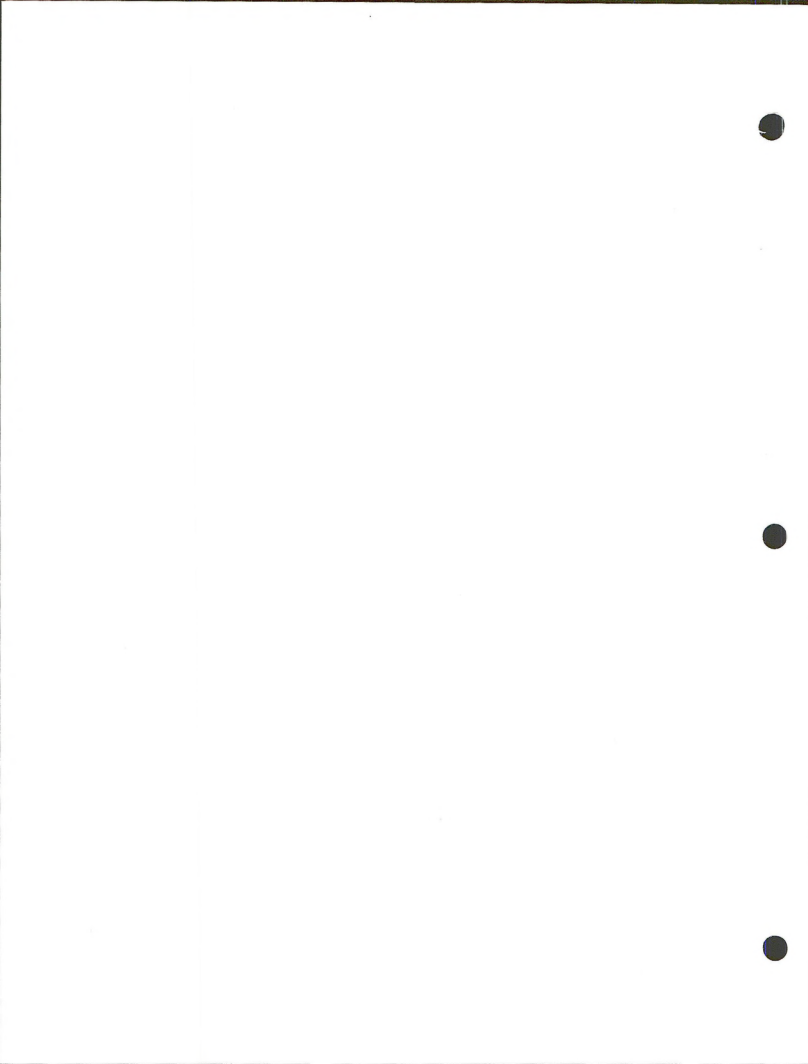
## Influenza

### VACCINE AVAILABILITY

The revision of the ACIP influenza vaccine recommendations is released annually through the Montana Morbidity Mortality Weekly Report, usually in the summer.

Influenza vaccine is NOT available directly from the Immunization Program due to termination of the federally funded grant in 1983. The Montana Department of Administration does solicit a contract price which local public providers may use. Notice of that contract price and contract number is sent to local providers in the summer prior to the influenza season. An influenza Important Information Form is prepared annually and a copy available upon request to the Montana Immunization Program.

(See the attached ACIP statement). Also, refer to the Adult Immunization Recommendation on influenza and the Control of Communicable Diseases in Man.



Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Prevention and Control of Influenza: Part I, Vaccines**

These recommendations update information on the vaccine available for controlling influenza during the 1989-90 influenza season (superseding *MMWR* 1988;37: 361-73). Changes include statements about 1) updating of the influenza strains in the trivalent vaccine for 1989-90, 2) revision of the high-priority groups for immunization, 3) increased emphasis on the need for vaccination of health-care workers and household contacts of high-risk persons, 4) vaccination for travelers, and 5) review of strategies for reaching high-risk groups with vaccine.

Antiviral agents also have an important role in the control of influenza. Recommendations for the use of antiviral agents will be published in the summer or fall of 1989 as Part II of these recommendations.

**INTRODUCTION**

Influenza A viruses are classified into subtypes on the basis of two antigens: hemagglutinin (H) and neuraminidase (N). Three subtypes of hemagglutinin (H1, H2, H3) and two subtypes of neuraminidase (N1, N2) are recognized among influenza A viruses that have caused widespread human disease. Immunity to these antigens, especially the hemagglutinin, reduces the likelihood of infection and lessens the severity of disease if infection occurs. However, over time, there may be enough antigenic variation (antigenic drift) within the same subtype that infection or vaccination with one strain may not induce immunity to distantly related strains of the same subtype. Although influenza B viruses have shown more antigenic stability than influenza A viruses, antigenic variation does occur. For these reasons, major epidemics of respiratory disease caused by new variants of influenza continue to occur. The antigenic characteristics of current strains provide the basis for selecting virus strains included in each year's vaccine.

Typical influenza illness is characterized by abrupt onset of fever, sore throat, and nonproductive cough. Unlike many other common respiratory infections, influenza can cause extreme malaise lasting several days. More severe illness can result if the influenza virus invades the lungs (primary viral pneumonia) or if secondary bacterial pneumonia occurs. High attack rates of acute illness during influenza epidemics usually result in dramatic increases in visits to physicians' offices, walk-in clinics, and emergency rooms by persons of all ages and in increases in hospitalizations for management of lower-respiratory-tract complications.

Elderly persons and persons with underlying health problems are at increased risk for complications of influenza infection. Such high-risk persons are more likely than the general population to require hospitalization if infected. One recent study showed that, during major epidemics, hospitalization rates for high-risk adults increased twofold to fivefold, depending on age group. Previously healthy children and younger adults may also require hospitalization for influenza-related complications, but the relative increase in their hospitalization rates is less than for persons in high-risk groups.

An increase in mortality further indicates the impact of influenza epidemics. Increased mortality results from not only pneumonia but also cardiopulmonary or other chronic diseases that can be exacerbated by influenza infection. Ten thousand or more excess deaths have been documented in each of 19 different epidemics during 1957-1986; more than 40,000 excess deaths occurred in each of several recent epidemics. Approximately 80%-90% of the excess deaths attributed to pneumonia and influenza were among persons  $\geq 65$  years of age. However, influenza-associated deaths also occur in children and previously healthy adults  $< 65$  years of age during major epidemics.

Because the proportion of elderly persons in the U.S. population is increasing and because age and its associated chronic diseases are risk factors for severe influenza illness, the toll from influenza can be expected to increase unless control measures are used more vigorously. The number of younger

persons at high risk for infection-related complications is also increasing for various reasons, such as the success of neonatal intensive-care units, better management of diseases such as cystic fibrosis, and better survival rates for organ-transplant recipients.

#### **OPTIONS FOR THE CONTROL OF INFLUENZA**

Two measures are available in the United States to reduce the impact of influenza: immunoprophylaxis with inactivated (killed-virus) vaccine and chemoprophylaxis or therapy with an influenza-specific antiviral drug (a.g., amantadine). Vaccination of high-risk persons each year before the influenza season is the most important measure for reducing the impact of influenza. Vaccination can be highly cost-effective 1) when it is aimed at persons who are most likely to experience complications or who have a higher-than-average risk for exposure and 2) when it is administered to high-risk persons during a hospitalization or routine health-care visit before the influenza season, thus making special visits to physicians' offices or clinics unnecessary. Recent reports indicate that, when vaccine and epidemic strains of virus are well matched, achieving high vaccination rates in closed populations can reduce the risk of outbreaks by inducing herd immunity. When outbreaks of influenza A occur in closed populations, they can be interrupted by chemoprophylaxis for all residents. (Additional information on chemoprophylaxis will be published in the *MMWR* before the 1989-90 season.)

Other indications for immunization include the strong desire of any person to avoid an influenza infection, reduce the severity of disease, or reduce the chances of transmitting influenza to high-risk persons with whom they have frequent contact.

#### **INACTIVATED VACCINE FOR INFLUENZA A AND B**

Influenza vaccine is made from highly purified, egg-grown viruses that have been rendered noninfectious (inactivated). Influenza vaccine contains three virus strains (two type A and one type B) representing influenza viruses recently circulating worldwide and believed likely to circulate in the United States the following winter. The composition of the vaccine is such that it causes minimal systemic or febrile reactions. Whole-virus, subvirion, and purified surface antigen preparations are available. Only subvirion or purified surface antigen preparations should be used for children to minimize febrile reactions. Subvirion, purified surface antigen, or whole-virus vaccines may be used in adults. Most vaccinated children and young adults develop high postvaccination hemagglutination-inhibition antibody titers that are likely to protect them against infection by strains like those in the vaccine and often by related variants that may emerge. Elderly persons and persons with certain chronic diseases may develop lower postvaccination antibody titers than healthy young adults and thus may remain susceptible to influenza upper-respiratory-tract infection. Nevertheless, influenza vaccine can still be effective in preventing lower-respiratory-tract involvement or other complications, thereby reducing the risk of hospitalization and death.

#### **RECOMMENDATIONS FOR USE OF INACTIVATED INFLUENZA VACCINE**

Influenza vaccine is strongly recommended for any person  $\geq 6$  months of age who, by virtue of age or underlying medical condition, is at increased risk for complications of influenza. It is also strongly recommended for health-care workers and others (including household members) who may have close contact with high-risk persons. In addition, influenza vaccine may be given to any other person who wishes to reduce his/her chance of becoming infected with influenza, even if that person is not at increased risk for complications.

Vaccine composition and dosages for the 1989-90 season are given in Table 1. Guidelines for the use of vaccine among different groups are given below.

Although the current influenza vaccine often contains one or more antigens used in previous years, immunity declines in the year following vaccination. Therefore, annual vaccination using the current vaccine is required. Remaining 1988-89 vaccine should not be used to provide protection for the 1989-90 influenza season.

Two doses may be required for a satisfactory antibody response in previously unvaccinated children  $\leq 12$  years of age; however, clinical studies with vaccines similar to those in current use have shown only marginal or no improvement in antibody response when a second dose is given to adults during the same season.

During the past decade, data on influenza vaccine immunogenicity and side effects have generally been obtained when vaccine has been administered intramuscularly. Because there has been no adequate evaluation of recent influenza vaccines administered by other routes, the intramuscular route should be used. Adults and older children should be vaccinated in the deltoid muscle, and infants and young children, in the anterolateral aspect of the thigh.

## TARGET GROUPS FOR SPECIAL VACCINATION PROGRAMS

To maximize protection of high-risk persons, both the persons at risk and their close contacts should be targeted for organized vaccination programs.

### Groups at Increased Risk for Influenza-Related Complications

1. Adults and children with chronic disorders of the pulmonary or cardiovascular systems, including children with asthma.
2. Residents of nursing homes and other chronic-care facilities housing patients of any age with chronic medical conditions.
3. Persons  $\geq 65$  years of age.
4. Adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression.
5. Children and teenagers (aged 6 months–18 years) who are receiving long-term aspirin therapy and therefore may be at risk of developing Reye syndrome after an influenza infection.

### Groups Potentially Capable of Transmitting Influenza to High-Risk Persons

Persons attending high-risk persons can transmit influenza infections to them while they themselves are undergoing subclinical infection or working despite the existence of symptoms. Some high-risk persons (e.g., the elderly, transplant recipients, or persons with acquired immunodeficiency syndrome [AIDS]) can have relatively low antibody responses to influenza vaccine. Efforts to protect them against influenza may be improved by reducing the chances that their care providers may expose them to influenza. Therefore, the following groups should be vaccinated:

1. Physicians, nurses, and other personnel in both hospital and outpatient-care settings who have extensive contact with high-risk patients in all age groups, including infants.
2. Providers of home care to high-risk persons (e.g., visiting nurses, volunteer workers).
3. Household members (including children) of high-risk persons.

## VACCINATION OF OTHER GROUPS

### General Population

Physicians should administer influenza vaccine to any person who wishes to reduce his/her chances of acquiring influenza infection. Persons who provide essential community services and students or other persons in institutional settings (i.e., schools and colleges) may be considered for vaccination to minimize the disruption of routine activities during outbreaks.

### Pregnant Women

Influenza-associated excess mortality among pregnant women has not been documented, except in the largest pandemics of 1918–19 and 1957–58. However, pregnant women who have other medical conditions that increase their risk for complications from influenza should be vaccinated, as the vaccine is considered safe for pregnant women. Administering the vaccine after the first trimester is a reasonable precaution to minimize any concern over the theoretical risk of teratogenicity. However, it

TABLE 1. Influenza vaccine\* dosage, by patient age – United States, 1989–90 season

| Age group     | Product <sup>†</sup> | Dosage  | No. doses           | Route <sup>‡</sup> |
|---------------|----------------------|---------|---------------------|--------------------|
| 6–35 mos      | Split virus only     | 0.25 mL | 1 or 2 <sup>§</sup> | IM                 |
| 3–12 yrs      | Split virus only     | 0.50 mL | 1 or 2 <sup>§</sup> | IM                 |
| $\geq 12$ yrs | Whole or split virus | 0.50 mL | 1                   | IM                 |

\*Contains 15  $\mu$ g each of A/Taiwan/1/86-like (H1N1), A/Shanghai/11/87-like (H3N2), and B/Yamagata/16/88-like hemagglutinin antigens in each 0.5 mL. Manufacturers include: Connaught Laboratories, Inc. (distributed by E.R. Squibb & Sons Inc.) (Fluzone® whole or split); Parke-Davis (Fluogen® split); and Wyeth-Ayerst Laboratories (Influenza Virus Vaccine, Trivalent® split). For further product information call Connaught, (800) 822-2463; Parke-Davis, (800) 223-0432; Wyeth-Ayerst, (800) 321-2304. A fourth vaccine, manufactured by Evans Medicals Ltd. and distributed by Lederle Laboratories (purified surface antigen vaccine), may be available for the 1989-90 influenza season. Further information can be obtained from Lederle Laboratories, telephone [800] 533-3753.

<sup>†</sup>Because of the lower potential for causing febrile reactions, only split-virus vaccines should be used in children ("split virus" refers to viruses that have been chemically treated to reduce the level of potentially pyrogenic components). They may be labeled as "split," "subvirion," or "purified surface antigen" vaccine. Immunogenicity and side effects of split- and whole-virus vaccines are similar in adults when vaccines are used according to the recommended dosage.

<sup>‡</sup>The recommended site of vaccination is the deltoid muscle for adults and older children. The preferred site for infants and young children is the anterolateral aspect of the thigh.

<sup>§</sup>Two doses are recommended for children  $\leq 12$  years old who are receiving influenza vaccine for the first time.

is undesirable to delay vaccination of pregnant women with high-risk conditions who will still be in the first trimester of pregnancy when the influenza season begins.

#### **Persons Infected with HIV**

Increases in infections and complications caused by various respiratory pathogens have been observed in persons infected with HIV. However, similar increases due to influenza have not been reported during recent epidemics. Nevertheless, because influenza may result in serious illness and complications in some HIV-infected persons, vaccination is a prudent precaution.

#### **Foreign Travelers**

Increasingly, the elderly and persons with high-risk medical conditions are embarking on international travel. The risk of exposure to influenza during foreign travel varies, depending on, among other factors, season of travel and destination. Influenza can occur throughout the year in the tropics; the season of greatest influenza activity in the Southern Hemisphere is April–September. Because of the short incubation period for influenza, exposure to the virus during travel will often result in clinical illness that begins during travel, an inconvenience or potential danger, especially for persons at increased risk for complications. Persons preparing to travel to the tropics at any time of year or to the Southern Hemisphere during April–September should review their vaccination histories. If not vaccinated the previous fall/winter, they should be considered for influenza vaccination before travel. Persons in the high-risk categories especially should be encouraged to receive the vaccine. The most current available vaccine should be used. High-risk persons given the previous season's vaccine before travel should be revaccinated in the fall/winter with current vaccine.

#### **PERSONS WHO SHOULD NOT BE VACCINATED**

Inactivated influenza vaccine should not be given to persons known to have an anaphylactic hypersensitivity to eggs (see below: Side Effects and Adverse Reactions).

Persons with acute febrile illnesses usually should not be vaccinated until their symptoms have abated.

#### **SIDE EFFECTS AND ADVERSE REACTIONS**

*Because influenza vaccine contains only noninfectious viruses, it cannot cause influenza.* Occasional cases of respiratory disease following vaccination represent coincidental illnesses unrelated to influenza vaccination. The most frequent side effect of vaccination is soreness around the vaccination site for up to 2 days; this occurs in less than one third of vaccinees.

In addition, the following two types of systemic reactions have occurred:

1. Fever, malaise, myalgia, and other systemic symptoms occur infrequently and most often affect persons who have had no exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6–12 hours after vaccination and can persist for 1 or 2 days.
2. Immediate, presumably allergic, reactions (such as hives, angioedema, allergic asthma, or systemic anaphylaxis) occur extremely rarely after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component—most likely residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, this protein is presumed capable of inducing immediate hypersensitivity reactions in persons with severe egg allergy, and such persons should not be given influenza vaccine, including persons who develop hives, have swelling of the lips or tongue, or experience acute respiratory distress or collapse after eating eggs. Persons with a documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses from occupational exposure to egg protein, may also be at increased risk for reactions from influenza vaccine.

Unlike the 1976 swine influenza vaccine, subsequent vaccines prepared from other virus strains have not been associated with an increased frequency of Guillain-Barré syndrome. Although influenza vaccination can inhibit the clearance of warfarin and theophylline, clinical studies have consistently failed to show any adverse effects attributable to these drugs in patients receiving influenza vaccine.

#### **SIMULTANEOUS ADMINISTRATION OF OTHER VACCINES, INCLUDING CHILDHOOD VACCINES**

The target groups for influenza and pneumococcal vaccination overlap considerably. Both vaccines can be given at the same time at different sites without increasing side effects. However, influenza vaccine must be given annually, and with few exceptions, pneumococcal vaccine should be given only once.

High-risk children usually see a health professional to receive routine pediatric vaccines. These visits provide a good opportunity to administer influenza vaccine simultaneously but in a different site.



Although studies have not been conducted, simultaneous administration should not diminish immunogenicity or increase adverse reactions.

#### **TIMING OF INFLUENZA VACCINATION ACTIVITIES**

Influenza vaccine may be offered to high-risk persons presenting for routine care or hospitalization beginning in September but not until new vaccine is available. Except in years of pandemic influenza (e.g., 1957 and 1968), high levels of influenza activity generally do not occur in the contiguous 48 states before December. Therefore, organized vaccination campaigns in which high-risk persons are routinely accessible are *optimally* undertaken in November. In facilities such as nursing homes, it is particularly important to avoid administering vaccine too far in advance of the influenza season because antibody level begins to decline within a few months. Such vaccination programs may be undertaken as soon as current vaccine is available in September or October if regional influenza activity is expected to begin earlier than usual.

Children  $\leq 12$  years of age who have not been vaccinated previously should receive two doses at least 1 month apart to maximize the chance of a satisfactory antibody response to all three vaccine antigens. The second dose should be given before December, if possible. Vaccine should continue to be offered to both children and adults up to and even after influenza virus activity is documented in a community, which may be as late as April in some years.

#### **STRATEGIES FOR IMPLEMENTING INFLUENZA VACCINE RECOMMENDATIONS**

Despite the recognition that optimum medical care for both adults and children includes regular review of immunization records and administration of vaccines as appropriate, in recent years, an average of  $<30\%$  of persons in high-risk groups have received influenza vaccine each year. More effective strategies for delivering vaccine to high-risk persons, their health-care providers, and their household contacts are clearly needed.

In general, successful vaccination programs have been those that have combined education for health-care workers, publicity and education targeted toward potential recipients, a routine for identifying (usually by medical record review) persons at risk, and efforts to remove administrative and financial barriers that prevent persons from receiving the vaccine.

Persons for whom influenza vaccine is recommended can be identified and immunized in the following settings:

##### **Outpatient Clinics and Physicians' Offices**

Staff in physicians' offices, clinics, health maintenance organizations, and employee health clinics should be instructed to identify and mark the medical records of patients who should receive vaccine. Vaccine should be offered during visits beginning in September and continuing through the influenza season. Offer of vaccine and its receipt or refusal should be documented in the medical record. Patients in high-risk groups who do not have regularly scheduled visits during the fall should be reminded by mail or telephone of the need for vaccine, and if possible, arrangements should be made to provide vaccine with minimal waiting time and at the lowest possible cost.

##### **Facilities Providing Episodic or Acute Care (e.g., emergency rooms, walk-in clinics)**

Health-care providers in these settings should be familiar with influenza vaccine recommendations and should offer vaccine to persons in high-risk groups or should provide written information on why, where, and how to obtain the vaccine. Written information should be available in Spanish or other language(s) appropriate for the population served by the facility.

##### **Nursing Homes and Other Residential Long-Term Care Facilities**

Immunization should be routinely provided to residents of chronic-care facilities, with concurrence of physicians, rather than by procuring orders for administration of vaccine for each patient. Consent for immunization should be obtained at the time of admission to the facility, and all residents immunized at one period of time immediately preceding the influenza season. Residents admitted after completion of the vaccination program should be immunized at the time of admission during the winter months.

##### **Acute-Care Hospitals**

Patients of any age in medically high-risk groups and all persons  $\geq 65$  years of age who are hospitalized from September through March should be offered and strongly encouraged to receive vaccine before discharge. Household members and others with whom they will have contact should receive written information about reasons they should also receive influenza vaccine and places to obtain the vaccine.

**Outpatient Facilities Providing Continuing Care to High-Risk Patients** (e.g., hemodialysis centers, hospital specialty-care clinics, outpatient rehabilitation programs)

All patients should be offered vaccine at one period of time shortly before the beginning of the influenza season. Patients admitted during the winter months after the vaccination program should be immunized at the time of admission for care. Household members should receive written information regarding need for immunization and places to obtain the vaccine.

**Visiting Nurses and Others Providing Home Care to High-Risk Persons**

Nursing-care plans should identify high-risk patients, and vaccine should be provided in the home if necessary. Caregivers and others in the household should be referred for immunization.

**Facilities Providing Services to Persons  $\geq 65$  Years of Age** (e.g., retirement communities, recreation centers)

If possible, all unimmunized residents/attendees should be offered vaccine on site at one time period before the influenza season; alternatively, education/publicity programs should emphasize need for vaccine and should provide specific information on how, where, and when to obtain it.

**Clinics and Others Providing Health Care for Travelers**

Indications for influenza vaccine should be reviewed before travel and vaccine offered if appropriate (see previous section: Vaccination for Foreign Travelers).

**Health-Care Workers**

Administrators of all of the above facilities and organizations should arrange for influenza vaccine to be offered to all personnel before the influenza season. Personnel should be provided with appropriate educational materials and strongly encouraged to receive vaccine, with particular emphasis on immunization of persons caring for highest-risk patients (i.e., staff of intensive-care units [including newborn intensive-care units] and chronic-care facilities). Use of a mobile cart to take vaccine to hospital wards or other worksites, and availability of vaccine during night and weekend workshifts may enhance compliance, as may a follow-up campaign if an outbreak threatens.

#### **SOURCES OF INFORMATION ON INFLUENZA-CONTROL PROGRAMS**

Educational materials about influenza and its control are available from a variety of sources, including CDC. For information on sources of educational materials, contact Technical Information Services, Center for Prevention Services, Mailstop E-07, CDC, Atlanta, GA 30333.

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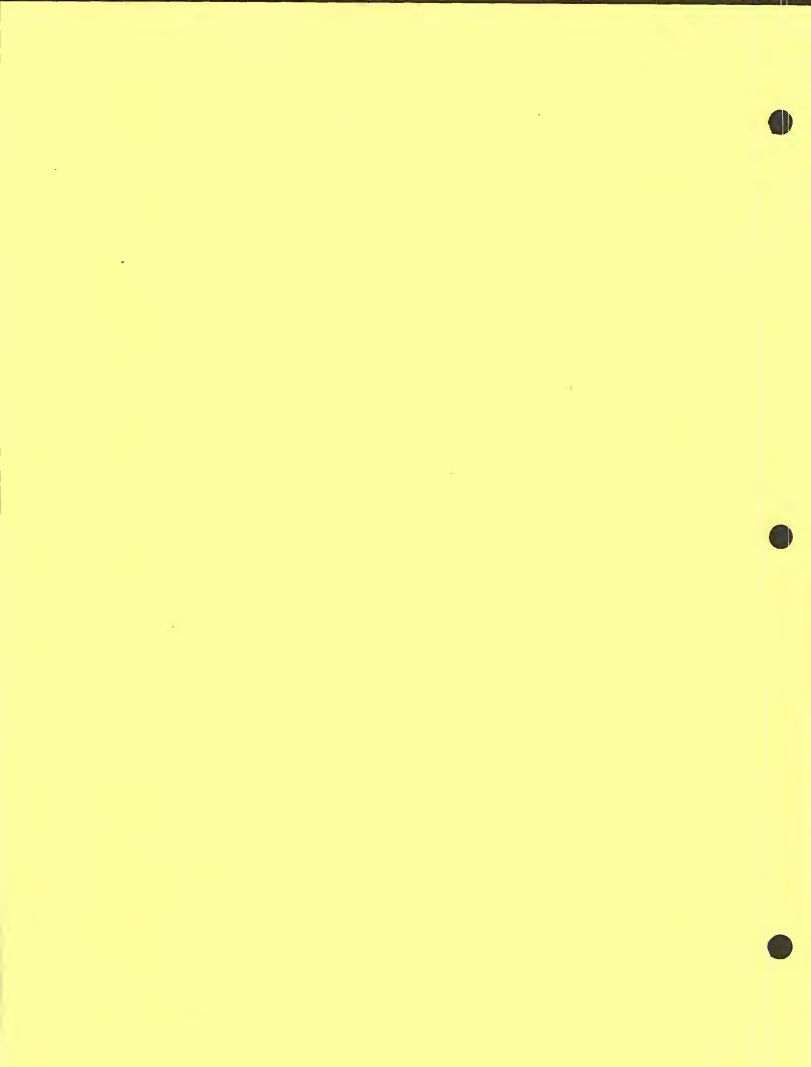
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# IMPORTANT INFORMATION ABOUT INFLUENZA AND INFLUENZA VACCINE, 1989 - 1990

PLEASE READ THIS CAREFULLY

**WHAT IS INFLUENZA ("FLU")?** Influenza (or "flu") is a viral infection of the nose, throat, bronchial tubes, and lungs that can make someone of any age ill. Usually the flu occurs in the United States from about November to April. If you get the flu, you usually have fever, chills, cough, and soreness and aching in your back, arms, and legs. Although most people are ill for only a few days, some persons have a much more serious illness and may need to go to the hospital. On average, thousands of people die each year in the United States from the flu or related complications.

**WHO SHOULD GET INFLUENZA VACCINE?** Because influenza is usually not life threatening in healthy individuals and most people recover fully, health officials emphasize the use of vaccine for the elderly and people with other health problems which make these individuals more likely to be seriously ill or to die from the flu or its complications. For example, people who after even light exercise become short of breath due to diseases affecting their heart or lungs, and people who have low resistance to infections, are likely to be more seriously affected by the flu. Thus, the following groups are at increased risk for serious illness with the flu and should receive vaccine:

- Adults and children with long-term heart or lung problems which caused them to see a doctor regularly, or to be

admitted to a hospital for care during the past year.

- Residents of nursing homes, and other institutions housing patients of any age who have serious long-term health problems.
- Healthy people over 65 years of age.
- People of any age who during the past year have regularly seen a doctor or have been admitted to a hospital for treatment for kidney disease, cystic fibrosis, diabetes, anemia ("low blood"), or severe asthma.
- People who have a type of cancer or immunological disorder (or use certain types of medicines) that lowers the body's normal resistance to infections. (Because influenza might cause serious illness and complications in persons infected with the AIDS virus, these individuals should receive influenza vaccine.)
- Children and teenagers (6 months through 18 years of age) on long-term treatment with aspirin who, if they catch the flu, may be at risk of getting Reye syndrome (a childhood disease that causes coma, liver damage, and death).

(PLEASE READ OTHER SIDE)

Certain medical staff who provide care to high-risk patients in health-care facilities should be vaccinated, to reduce the possibility that these patients might catch the flu when receiving medical care. Family members or others who provide care to high-risk persons at home should also be vaccinated. The possibility for spreading the flu to high-risk persons can be reduced by vaccinating:

- Doctors, nurses, and others in both hospital and outpatient-care settings who have extensive contact with high-risk patients in all age groups, including children.
- Individuals who provide care to high-risk persons at home, such as visiting nurses and volunteers, as well as all household members, including children, whether or not they are providers of care.

In addition, a flu shot may be given to:

- Persons wishing to reduce their chances of catching the flu.
- Persons who provide essential community services.
- Students or other persons in schools and colleges if outbreaks would cause major disruptions of school activities.
- Persons traveling to the tropics at any time of the year or to countries south of the equator during April-September. (Persons with high-risk medical conditions and those ages 65 and older who are traveling as indicated above especially should be encouraged to receive vaccine.)

**INFLUENZA VACCINE:** The viruses that cause flu frequently change, so people who have been infected or given a flu shot in previous years may become infected with a new strain. Because of this, and because any immunity produced by the flu shot will possibly decrease in the year after vaccination, persons in the high-risk groups listed above should be vaccinated every year. This year's flu shot contains the strains A/Taiwan/1/86, A/Shanghai/11/87, and B/Yamagata/16/88 to provide immunity against the types of flu which have been circulating in the past year, and/or are thought to be most likely to occur in the United States next winter. All the viruses in the vaccine are killed so that they cannot infect anyone. Vaccine will begin to provide its protective effect after about one or two weeks, and immunity may decrease, on average, after several months.

Flu shots will not protect all persons who get them against the flu. They also will not protect against other illnesses that resemble the flu.

**DOSAGE:** Only a single flu shot is needed each season for persons older than 12 years, but children 12 years or less may need a second shot after about a month. The doctor or nurse giving the flu shot will discuss this with parents or guardians. Children should be given only vaccine that has been chemically treated during manufacture (split virus) to reduce chances of any side effects. Split-virus vaccines can also be used by adults.

**POSSIBLE SIDE EFFECTS FROM THE VACCINE:** Most people have no side effects from recent influenza vaccines. Flu shots are given by injection, usually into a muscle of the upper arm. This may cause soreness for a day or two at the injection site and occasionally may also cause a fever or achiness for one or two days. Unlike 1976 swine flu vaccine, recent flu shots have not been linked to the paralytic illness Guillain Barre syndrome. As is the case with most drugs or vaccines, there is a possibility that allergic or more serious reactions, or even death, could occur with the flu shot.

**WARNING-SOME PEOPLE SHOULD CHECK WITH A DOCTOR BEFORE TAKING INFLUENZA VACCINE:**

- Persons who should not be given the flu shot include those with an allergy to eggs that causes dangerous reactions if they eat eggs.
- Anyone who has ever been paralyzed with Guillain Barre syndrome should seek advice from their doctor about special risks that might exist in their cases.
- Women who are or might be pregnant should consult with their doctor.
- Persons who are ill and have a fever should delay vaccination until the fever and other temporary symptoms have gone.

**QUESTIONS:** If you have any questions about influenza or influenza vaccination, please ask now or call your doctor before requesting the vaccine.

**REACTIONS:** If anyone receiving influenza vaccine gets sick and visits a doctor, hospital, or clinic in the 4-weeks after vaccination, please report this to:

**PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS**

Influenza 7/1/89

*I have read or have had explained to me the information on this form about influenza and influenza vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of influenza vaccine and request that the vaccine be given to me or to the person named below for whom I am authorized to make this request.*

**INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)**

**FOR CLINIC USE**

|   |             |               |                                |                         |  |                     |
|---|-------------|---------------|--------------------------------|-------------------------|--|---------------------|
| Name (Please Print) _____   |             |               |                                | Birthdate _____         | Age _____  | Clinic Ident. _____ |
| Last _____  | First _____ | Initial _____ | City _____                     | Date Vaccinated _____   |  |                     |
| Address _____   |             |               |                                | City _____              | Date Vaccinated _____  |                     |
| County _____  | State _____ | Zip _____     | Manufacturer and Lot No. _____ |                         |  |                     |
| X _____   |             |               |                                | Site of Injection _____ |  |                     |
| Signature of Person to receive (or person authorized to make the request) |             |               |                                | Date _____              | Chronic Disease Yes <input type="checkbox"/> No <input type="checkbox"/> |                     |

Pneumococcal

VACCINE AVAILABILITY

The Montana Immunization Program does not provide pneumococcal vaccine, but the Immunization Program will solicit bids through the Department of Administration for a term contract price for public providers. Notices are sent to local providers of regarding the term contract (contract price, contract number and ordering instructions).

(See the attached ACIP statement and Important Information Form). Also, refer to the Adult Immunization Recommendation on Pneumococcal disease and the Control of Communicable Diseases in Man.





Recommendations of the Immunization  
Practices Advisory Committee

**Pneumococcal Polysaccharide Vaccine**

*These recommendations update the last statement by the Immunization Practices Advisory Committee (ACIP) on pneumococcal polysaccharide vaccine (MMWR 1984;33:273-6, 281) and include new information regarding 1) vaccine efficacy, 2) use in persons with human immunodeficiency virus (HIV) infection and in other groups at increased risk of pneumococcal disease, and 3) guidelines for revaccination.*

**INTRODUCTION**

Disease caused by *Streptococcus pneumoniae* (pneumococcus) remains an important cause of morbidity and mortality in the United States, particularly in the very young, the elderly, and persons with certain high-risk conditions. Pneumococcal pneumonia accounts for 10%–25% of all pneumonias and an estimated 40,000 deaths annually (1). Although no recent data from the United States exist, in the United Kingdom pneumococcal infections may account for 34% of pneumonias in adults who require hospitalization (2). The best estimates of the incidence of serious pneumococcal disease in the United States are based on surveys and community-based studies of pneumococcal bacteremia. Recent studies suggest annual rates of bacteremia of 15–19/100,000 for all persons, 50/100,000 for persons  $\geq 65$  years old, and 160/100,000 for children  $\leq 2$  years old (3,4). These rates are 2–3 times those previously documented in the United States. The overall rate for pneumococcal bacteremia in some Native American populations can be six times the rate of the general population (5). The incidence of pneumococcal pneumonia can be 3–5 times that of the detected rates of bacteremia. The estimated incidence of pneumococcal meningitis is 1–2/100,000 persons.

Mortality from pneumococcal disease is highest in patients with bacteremia or meningitis, patients with underlying medical conditions, and older persons. In some high-risk patients, mortality has been reported to be  $>40\%$  for bacteremic disease and 55% for meningitis, despite appropriate antimicrobial therapy. Over 90% of pneumococci remain very sensitive to penicillin.

In addition to the very young and persons  $\geq 65$  years old, patients with certain chronic conditions are at increased risk of developing pneumococcal infection and severe pneumococcal illness. Patients with chronic cardiovascular diseases, chronic pulmonary disease, diabetes mellitus, alcoholism, and cirrhosis are generally immunocompetent but have increased risk. Other patients at greater risk because of decreased responsiveness to polysaccharide antigens or more rapid decline in serum antibody include those with functional or anatomic asplenia (e.g., sickle cell disease or splenectomy), Hodgkin's disease, lymphoma, multiple myeloma, chronic renal failure, nephrotic syndrome, and organ transplantation. In a recent population-based study, all persons 55–64 years old with pneumococcal bacteremia had at least one of these chronic conditions (4). Studies indicate that patients with acquired immunodeficiency syndrome (AIDS) are also at increased risk of pneumococcal disease, with an annual attack rate of pneumococcal pneumonia as high as 17.9/1000 (6–8). This observation is consistent with the B-cell dysfunction noted in patients with AIDS (9,10). Recurrent pneumococcal meningitis may occur in patients with cerebrospinal fluid leakage complicating skull fractures or neurologic procedures.

**PNEUMOCOCCAL POLYSACCHARIDE VACCINE**

The current pneumococcal vaccine (Pneumovax<sup>®</sup> 23, Merck Sharp & Dohme, and Pnu-Imune<sup>®</sup> 23, Lederle Laboratories) is composed of purified capsular polysaccharide antigens of 23 types of *S. pneumoniae* (Danish types 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F). It was licensed in the United States in 1983, replacing a 14-valent vaccine licensed in 1977. Each vaccine dose (0.5 mL) contains 25  $\mu\text{g}$  of each polysaccharide antigen. The 23 capsular

types in the vaccine cause 88% of the bacteremic pneumococcal disease in the United States. In addition, studies of the human antibody response indicate that cross-reactivity occurs for several types (e.g., 6A and 6B) that cause an additional 8% of bacteremic disease (11).

Most healthy adults, including the elderly, show a twofold or greater rise in type-specific antibody, as measured by radioimmunoassay, within 2-3 weeks of vaccination. Similar antibody responses have been reported in patients with alcoholic cirrhosis and diabetes mellitus requiring insulin. In immunocompromised patients, the response to vaccination may be less. In children <2 years old, antibody response to most capsular types is generally poor. In addition, response to some important pediatric pneumococcal types (e.g., 6A and 14) is decreased in children <5 years old (12,13).

Following vaccination of healthy adults with polyvalent pneumococcal vaccine, antibody levels for most pneumococcal vaccine types remain elevated at least 5 years; in some persons, they fall to prevaccination levels within 10 years (14,15). A more rapid decline in antibody levels may occur in children. In children who have undergone splenectomy following trauma and in those with sickle cell disease, antibody titers for some types can fall to prevaccination levels 3-5 years after vaccination (16,17). Similar rates of decline can occur in children with nephrotic syndrome (18).

Patients with AIDS have been shown to have an impaired antibody response to pneumococcal vaccine (10,19). However, asymptomatic HIV-infected men or those with persistent generalized lymphadenopathy respond to the 23-valent pneumococcal vaccine (20).

#### VACCINE EFFICACY

In the 1970s, pneumococcal vaccine was shown to reduce significantly the occurrence of pneumonia in young, healthy populations in South Africa and Papua New Guinea, where incidence of pneumonia is high (21,22). It was also demonstrated to protect against systemic pneumococcal infection in hyposplenic patients in the United States (23). Since then, studies have attempted to assess vaccine efficacy in other U.S. populations (24-30; CDC, unpublished data) (Table 1). A prospective, ongoing case-control study in Connecticut has shown an overall protective efficacy of 61% against pneumococcal bacteremia caused by vaccine- and vaccine-related serotypes. The protective efficacy was 60% for patients with alcoholism or chronic pulmonary, cardiac, or renal disease and 64% for patients ≥55 years old without other high-risk chronic conditions (25,26). In another multicenter case-control study, vaccine efficacy in immunocompetent persons ≥55 years old was 70% (27). A smaller case-control study of veterans failed to show efficacy in preventing pneumococcal bacteremia (28), but determination of the vaccination status was judged to be inadequate and the selection of controls was considered to be potentially biased.

Studies based on CDC's pneumococcal surveillance system suggest an efficacy of 60%-64% for vaccine-type strains in patients with bacteremic disease. For all persons ≥65 years of age (including persons with chronic heart disease, pulmonary disease, or diabetes mellitus), vaccine efficacy was

TABLE 1. Clinical effectiveness of pneumococcal vaccination in U.S. populations

| Location                  | Method                                   | No. persons                         | Type infection               | Vaccine efficacy (%)                 | 95% C.I.                                       |
|---------------------------|--|-------------------------------------|------------------------------|--------------------------------------|--|
| Connecticut (25,26)       | Case-control*                            | 543 cases<br>543 controls           | VT <sup>†</sup> , VT-related | 61                                   | 42, 73   |
| Philadelphia (27)         | Case-control*                            | 122 cases<br>244 controls           | All serotypes                | 70                                   | 37, 86   |
| Denver (28)               | Case-control*                            | 89 cases<br>89 controls             | All serotypes                | -21                                  | -221, 55                                       |
| CDC-1 (29)                | Epidemiologic*                           | 249 vaccinated<br>1638 unvaccinated | VT                           | 64                                   | 47, 76   |
| CDC-2 (unpublished)       | Epidemiologic*                           | 240 vaccinated<br>1527 unvaccinated | VT                           | 60                                   | 45, 70   |
| VA cooperative study (30) | Randomized controlled trial <sup>‡</sup> | 1145 vaccinated<br>1150 controls    | All serotypes<br>VT          | -34 <sup>§</sup><br>-19 <sup>§</sup> | -119, 18 <sup>§</sup><br>-164, 47 <sup>§</sup> |

\*Only patients with isolates from normally sterile body sites were included.

<sup>†</sup>Vaccine-type pneumococcal infection.

<sup>‡</sup>Pneumococcal pneumonia and bronchitis were diagnosed primarily by culture of respiratory secretions.

<sup>§</sup>Values calculated from the published data.

44%–61% (29; CDC, unpublished data). In addition, estimates of vaccine efficacy for serologically related types were 29%–66% (29). Limited data suggest that clinical efficacy may decline  $\geq 6$  years after vaccination (CDC, unpublished data).

A randomized, double-blind, placebo-controlled trial among high-risk veterans showed no vaccine efficacy against pneumococcal pneumonia or bronchitis (30); however, case definitions used were judged to have uncertain specificity. In addition, this study had only a 6% ability to detect a vaccine efficacy of 65% for pneumococcal bacteremia (31). In contrast, a French clinical trial found pneumococcal vaccine to be 77% effective in reducing the incidence of pneumonia in nursing home residents (32).

Despite conflicting findings, the data continue to support the use of the pneumococcal vaccine for certain well-defined groups at risk.

#### RECOMMENDATIONS FOR VACCINE USE

##### Adults

1. Immunocompetent adults who are at increased risk of pneumococcal disease or its complications because of chronic illnesses (e.g., cardiovascular disease, pulmonary disease, diabetes mellitus, alcoholism, cirrhosis, or cerebrospinal fluid leaks) or who are  $\geq 65$  years old.
2. Immunocompromised adults at increased risk of pneumococcal disease or its complications (e.g., persons with splenic dysfunction or anatomic asplenia, Hodgkin's disease, lymphoma, multiple myeloma, chronic renal failure, nephrotic syndrome, or conditions such as organ transplantation associated with immunosuppression).
3. Adults with asymptomatic or symptomatic HIV infection.

##### Children

1. Children  $\geq 2$  years old with chronic illnesses specifically associated with increased risk of pneumococcal disease or its complications (e.g., anatomic or functional asplenia [including sickle cell disease], nephrotic syndrome, cerebrospinal fluid leaks, and conditions associated with immunosuppression).
2. Children  $\geq 2$  years old with asymptomatic or symptomatic HIV infection.
3. The currently available 23-valent vaccine is **not** indicated for patients having only recurrent upper respiratory tract disease, including otitis media and sinusitis.

##### Special Groups

Persons living in special environments or social settings with an identified increased risk of pneumococcal disease or its complications (e.g., certain Native American populations).

#### ADVERSE REACTIONS

Approximately 50% of persons given pneumococcal vaccine develop mild side effects, such as erythema and pain at the injection site. Fever, myalgia, and severe local reactions have been reported in  $<1\%$  of those vaccinated. Severe systemic reactions, such as anaphylaxis, rarely have been reported.

#### PRECAUTIONS

The safety of pneumococcal vaccine for pregnant women has not been evaluated. Ideally, women at high risk of pneumococcal disease should be vaccinated before pregnancy.

#### TIMING OF VACCINATION

When elective splenectomy is being considered, pneumococcal vaccine should be given at least 2 weeks before the operation, if possible. Similarly, for planning cancer chemotherapy or immunosuppressive therapy, as in patients who undergo organ transplantation, the interval between vaccination and initiation of chemotherapy or immunosuppression should also be at least 2 weeks.

#### REVACCINATION

In one study, local reactions after revaccination in adults were more severe than after initial vaccination when the interval between vaccinations was 13 months (33) (Table 2). Reports of revaccination after longer intervals in children and adults, including a large group of elderly persons revaccinated at least 4 years after primary vaccination, suggest a similar incidence of such reactions after primary vaccination and revaccination (unpublished data; 17,34–38).

Without more information, persons who received the 14-valent pneumococcal vaccine should not be routinely revaccinated with the 23-valent vaccine, as increased coverage is modest and duration of protection is not well defined. However, revaccination with the 23-valent vaccine should be strongly considered for persons who received the 14-valent vaccine if they are at highest risk of fatal

pneumococcal infection (e.g., asplenic patients). Revaccination should also be considered for adults at highest risk who received the 23-valent vaccine  $\geq 6$  years before and for those shown to have rapid decline in pneumococcal antibody levels (e.g., patients with nephrotic syndrome, renal failure, or transplant recipients). Revaccination after 3–5 years should be considered for children with nephrotic syndrome, asplenia, or sickle cell anemia who would be  $\leq 10$  years old at revaccination.

#### STRATEGIES FOR VACCINE DELIVERY

Recommendations for pneumococcal vaccination have been made by the ACIP, the American Academy of Pediatrics, the American College of Physicians, and the American Academy of Family Physicians. Recent analysis indicates that pneumococcal vaccination of elderly persons is cost-effective (39). The vaccine is targeted for approximately 27 million persons aged  $\geq 65$  years and 21 million persons aged  $< 65$  years with high-risk conditions (1). Despite Medicare reimbursement for costs of the vaccine and its administration, which began in 1981, annual use of pneumococcal vaccine has not increased above levels observed in earlier years (40) (Figure 1). In 1985,  $< 10\%$  of the 48 million persons considered to be at increased risk of serious pneumococcal infection were estimated to have ever received pneumococcal vaccine (1).

Opportunities to vaccinate high-risk persons are missed both at time of hospital discharge and during visits to clinicians' offices. Two thirds or more of patients with serious pneumococcal disease had been hospitalized at least once within 5 years before their pneumococcal illness, yet few had received pneumococcal vaccine (40). More effective programs for vaccine delivery are needed, including offering pneumococcal vaccine in hospitals (at the time of discharge), clinicians' offices, nursing homes, and other chronic-care facilities. Many patients who receive pneumococcal vaccine should also be immunized with influenza vaccine (41), which can be given simultaneously at a different site. In contrast to pneumococcal vaccine, influenza vaccine is given annually.

#### VACCINE DEVELOPMENT

A more immunogenic pneumococcal vaccine preparation is needed, particularly for children  $< 2$  years old. The development of a protein-polysaccharide conjugate vaccine for selected capsular types holds promise.

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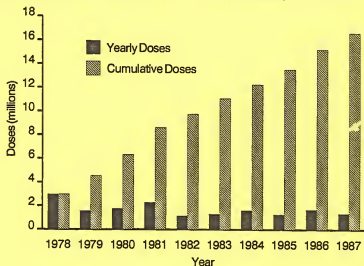
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TABLE 2. Reactions to revaccination with pneumococcal vaccine

| Study                         | Vaccinees           |              |     | Revaccination period | Reactions  |
|-------------------------------|---------------------|--------------|-----|----------------------|--|
|                               | Condition           | Age          | No. |                      |  |
| Borgono, et al. 1978 (33)     | Normal              | Adults       | 7   | 13 mos               | Increase in local reactions                                |
| Carlson, et al. 1979 (34)     | Normal              | 21–62 yrs    | 23  | 12–18 mos            | Increase in local reactions                                |
| Rigau-Perez, et al. 1983 (35) | Sickle cell disease | $\geq 3$ yrs | 28  | 28–35 mos            | No increase in reactions compared with primary vaccination |
| Lawrence, et al. 1983 (36)    | Normal              | 2–5 yrs      | 52  | 35 mos (mean)        | Increase in local reactions                                |
| Mufson, et al. 1984 (37)      | Normal              | 23–40 yrs    | 12  | 24–48 mos            | No increase in reactions compared with primary vaccination |
| Weinrub, et al. 1984 (17)     | Sickle cell disease | 10–27 yrs    | 17  | 8–9 yrs              | No "serious" local reactions                               |
| Kaplan, et al. 1986 (38)      | Sickle cell disease | 4–23 yrs     | 86  | 37–53 mos            | Four "severe" reactions*                                   |

\*Severe reaction was defined as presence of local pain, redness, swelling and axillary temperature  $> 100$  F (38.9 C); two patients aged 21 and 23 years had temperatures of 102 F (38.9 C).

FIGURE 1. Pneumococcal vaccine distribution — United States, 1978–1987\*



\*Data for 1978–1985 were obtained from reference 40. Data for 1986 and 1987 were obtained from Lederle Laboratories and Merck Sharp & Dohme (net doses distributed).

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# IMPORTANT INFORMATION ABOUT PNEUMOCOCCAL DISEASE AND PNEUMOCOCCAL POLYSACCHARIDE VACCINE

*Please read this carefully*

PNEUMOCOCCAL  
3/1/86

**WHAT IS PNEUMOCOCCAL DISEASE?** *Streptococcus pneumoniae* is a bacterium that causes much illness and death in the United States each year. This bacterium, also called the Pneumococcus, can cause serious infections of the lungs (pneumonia), the bloodstream (bacteremia), and the covering of the brain (meningitis). About 5 persons out of every 100 who get pneumococcal pneumonia, about 20 out of every 100 who get bacteremia, and about 30 out of every 100 who get meningitis die of these infections. Anyone can get pneumococcal disease; however, persons over 65 years of age and persons of any age who have special types of health problems have the greatest risk.

People are more likely to die from pneumococcal disease if they have problems such as alcoholism, heart or lung disease, kidney failure, diabetes, or certain types of cancer. Older persons as a group are also more likely to die from pneumococcal disease. Forty out of every 100 persons who have these special health problems die when they develop pneumococcal bacteremia and 55 out of 100 with these special health problems die if they get pneumococcal meningitis. The high risk of death occurs in spite of treatment with drugs like penicillin. Because of the risk of serious complications from pneumococcal infection, vaccination is recommended for older persons and for children and adults with special health problems.

#### **PNEUMOCOCCAL POLYSACCHARIDE VACCINE:**

The pneumococcal polysaccharide vaccine contains material

from the 23 types of pneumococcal bacteria that cause 87 percent of pneumococcal bacteremias. Most healthy adults who receive the vaccine develop protection against most or all of these types of pneumococcus bacteria 2-3 weeks after vaccination. Older persons and those with some long-term illnesses may not respond as well or at all. Children under 2 years of age are also not protected by the vaccine. How long the protection lasts is not known at this time; however, the vaccine should be given only once. The vaccine is given by injection.

#### **WHO SHOULD RECEIVE PNEUMOCOCCAL POLYSACCHARIDE VACCINE?**

Vaccination is recommended for the following:

##### **Adults**

1. Adults with long-term illnesses—especially those involving the heart or lungs.
2. Adults with long-term health problems that are associated with a high risk of getting serious pneumococcal infections. These include adults who have alcoholism, diabetes, kidney failure, abnormal function or removal of the spleen, Hodgkin's disease, multiple myeloma, cirrhosis, leaks of cerebrospinal fluid (CSF, the fluid surrounding the brain and spinal cord), or who have diseases that lower the body's resistance to infections or are taking drugs that lower the body's resistance to infections.

*(PLEASE READ OTHER SIDE)*

3. Older adults, especially those 65 years of age and older, who are otherwise healthy.

#### Children

Children 2 years of age and older with long-term illnesses that are associated with a high risk of getting serious pneumococcal infections. This includes children whose spleens have been surgically removed, as well as those who have sickle cell disease, nephrotic syndrome (a type of kidney disease), or CSF leaks, or who have diseases that lower the body's resistance to infections or are taking drugs that lower the body's resistance to infections.

#### Note

Frequent diseases of the upper respiratory system, including infections of the ear or sinuses, in children who are otherwise healthy, are *not* reasons to use this vaccine.

#### General Considerations

Although this vaccine may not be as effective in some persons, especially those who do not have normal resistance to infections, vaccination is still recommended for such persons because they are at high risk of developing severe disease.

#### POSSIBLE SIDE EFFECTS FROM THE VACCINE:

About half of those who are given pneumococcal vaccine have very mild side effects, such as redness and pain at the injection site. Less than 1 percent of those given pneumococcal vaccine may develop fever, muscle aches, and severe local reactions. Serious side effects, such as severe allergic reactions, have rarely been reported—about 5 in every million doses given. As with any drug or vaccine, there is a rare possibility that allergic or more serious reactions or even death could occur.

**RE Vaccination:** Pneumococcal vaccine should be given *only once* to adults; no "booster" dose is recommended. It is not yet known whether children need to be revaccinated. Allergic reactions have occurred among persons given second doses and are thought to be caused by existing immunity from the first dose. Persons who received the older pneumococcal vaccine that included only 14 types of pneumococcal bacteria do not need to receive this new vaccine since the slight increase in effectiveness does not outweigh the increased risk of reactions. Complete records of vaccination should be kept to avoid giving the vaccine more than once.

**Pregnancy:** The safety of pneumococcal vaccine for pregnant women has not been studied. It should not be given to healthy pregnant women. Women who are at high risk of pneumococcal disease and who are candidates for pneumococcal vaccine ideally should be vaccinated before pregnancy.

**Questions:** If you have any questions about pneumococcal disease or pneumococcal polysaccharide vaccine, please ask now or call your doctor or health department before you sign this form.

**Reactions:** If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic during the 4 weeks after receiving the vaccine, please report it to:

### PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS

*I have read the information on this form about pneumococcal disease and pneumococcal polysaccharide vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of the pneumococcal vaccine and request that it be given to me or to the person named below for whom I am authorized to make this request.*

PNEUMOCOCCAL  
3/1/86

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                      |            |       |           |      |
|---|------------|-------|-----------|------|
| Last Name   | First Name | MI    | Birthdate | Age  |
| Address   |            |       |           |      |
| City  | County     | State | Zip       |      |
| X   |            |       |           |      |
| Signature of person to receive vaccine or person authorized to make the request |            |       |           | Date |

| FOR CLINIC USE    |
|-------------------|
| Clinic Ident.     |
| Date Vaccinated   |
| Manuf and Lot No  |
| Site of injection |

#### FOR DATA PROCESSING USE ONLY (OPTIONAL)

| VACCINE HISTORY | PLACE CHECK              | IN BOX IF HISTORY PREVIOUSLY SUBMITTED  |   |   |   |          |  |
|-----------------|--------------------------|---|---|---|---|----------|--|
| DTP:            | <input type="checkbox"/> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | MEASLES: | MUMPS: <u>    </u> / <u>    </u> / <u>    </u>         |
| POLIO:          | <input type="checkbox"/> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | <u>    </u> / <u>    </u> / <u>    </u> | RUBELLA: | HAEMOPHILUS b: <u>    </u> / <u>    </u> / <u>    </u> |



## Hepatitis B

### VACCINE AVAILABILITY

The Montana Immunization Program does not provide Hepatitis B vaccine or immune globulin. State Term Contracts for purchasing Hepatitis B vaccine and Hepatitis B Immune Globulin (HBIG) are established through the State of Montana Department of Administration which allows a "vehicle" for public agencies to obtain the medications. Information related to the term contract is available through the Montana Immunization Program. Private resources for the hepatitis vaccine and immune globulin include hospitals, pharmacies and drug company representatives.

See ACIP statement and Important Information Form for Hepatitis B Vaccine. Also, refer to the Adult Immunization Recommendation on Hepatitis B and the Control of Communicable Diseases in Man.



Recommendation of the Immunization  
Practices Advisory Committee (ACIP)

**Recommendations for Protection Against Viral Hepatitis**

*The following statement updates all previous recommendations on use of immune globulins for protection against viral hepatitis (MMWR 1981;30:423-35) and use of hepatitis B vaccine and hepatitis B immune globulin for prophylaxis of hepatitis B (MMWR 1982;31:317-28 and MMWR 1984;33:285-90).*

**INTRODUCTION**

The term "viral hepatitis" is commonly used for several clinically similar diseases that are etiologically and epidemiologically distinct (1). Two of these, hepatitis A (formerly called infectious hepatitis) and hepatitis B (formerly called serum hepatitis) have been recognized as separate entities since the early 1940s and can be diagnosed with specific serologic tests. The third, currently known as non-A, non-B hepatitis, is probably caused by at least two different agents, and lacking specific diagnostic tests, remains a disease diagnosed by exclusion. It is an important form of acute viral hepatitis in adults and currently accounts for most posttransfusion hepatitis in the United States. An epidemic type of non-A, non-B hepatitis, which is probably spread by the fecal-oral route and is different from the types seen in the United States, has been described in parts of Asia and North Africa (2).

A fourth type of hepatitis, delta hepatitis, has recently been characterized as an infection dependent on hepatitis B virus. It may occur as a coinfection with acute hepatitis B infection or as superinfection of a hepatitis B carrier (3).

**HEPATITIS SURVEILLANCE**

Approximately 21,500 cases of hepatitis A, 24,300 cases of hepatitis B, 3,500 cases of non-A, non-B hepatitis, and 7,100 cases of hepatitis type unspecified were reported in the United States in 1983. Most cases of each type occur among young adults. Since reporting from many localities is incomplete, the actual number of hepatitis cases occurring annually is thought to be several times the reported number.

**IMMUNE GLOBULINS**

Immune globulins used in medical practice are sterile solutions of antibodies (immunoglobulins) from human plasma. They are prepared by cold ethanol fractionation of large plasma pools and contain 10%-18% protein. In the United States, plasma is primarily obtained from professional donors. Only plasma shown to be free of hepatitis B surface antigen (HBsAg) is used to prepare immune globulins.

Immune globulin (IG) (formerly called "immune serum globulin," ISG, or "gamma globulin") produced in the United States contains antibodies against the hepatitis A virus (anti-HAV) and the hepatitis B surface antigen (anti-HBs). Tests of IG lots prepared since 1977 indicate that both types of antibody have uniformly been present. Hepatitis B immune globulin (HBIG) is an IG prepared from plasma containing high titers of anti-HBs.

Neither IG nor HBIG commercially available in the United States transmits hepatitis or other viral infections. There is no evidence that the causative agent of AIDS (human T-lymphotropic virus type III/lymphadenopathy-associated virus [HTLV-III/LAV]) has been transmitted by IG or HBIG (4).

Serious adverse effects from immune globulins administered as recommended have been exceedingly rare. Standard immune globulins are prepared for intramuscular use and should not be given intravenously. Two preparations for intravenous use in immunodeficient and other selected patients have recently become available in the United States but are not recommended for hepatitis prophylaxis. Immune globulins are not contraindicated for pregnant women.

## HEPATITIS A

Hepatitis A is caused by the hepatitis A virus (HAV), a 27-nm ribonucleic acid (RNA) agent that is a member of the picornavirus family. The illness caused by HAV characteristically has an abrupt onset with fever, malaise, anorexia, nausea, abdominal discomfort, and jaundice. Severity is related to age. In children, most infections are asymptomatic, and illness is usually not accompanied by jaundice. Most infected adults become symptomatically ill with jaundice. Fatality among reported cases is infrequent (about 0.6%).

Hepatitis A is primarily transmitted by person-to-person contact, generally through fecal contamination. Transmission is facilitated by poor personal hygiene, poor sanitation, and intimate (intrahousehold or sexual) contact. Common-source epidemics from contaminated food and water also occur. Sharing utensils or cigarettes or kissing are not believed to transmit the infection.

The incubation period of hepatitis A is 15-50 days (average 28-30). High concentrations of HAV ( $10^9$  particles/g) are found in stools of infected persons. Fecal virus excretion reaches its highest concentration late in the incubation period and early in the prodromal phase of illness, and diminishes rapidly once jaundice appears. Greatest infectivity is during the 2-week period immediately before the onset of jaundice. Viremia is of short duration; virus has not been found in urine or other body fluids. A chronic carrier state with HAV in blood or feces has not been demonstrated. Transmission of HAV by blood transfusion has occurred but is rare.

The diagnosis of acute hepatitis A is confirmed by finding IgM-class anti-HAV in serum collected during the acute or early convalescent phase of disease. IgG-class anti-HAV, which appears in the convalescent phase of disease and remains detectable in serum thereafter, apparently confers enduring protection against disease. Commercial tests are available to detect IgM anti-HAV and total anti-HAV in serum.

Although the incidence of hepatitis A in the United States has decreased over the last 15 years, it is still a common infection in older children and young adults. About 38% of reported hepatitis cases in this country are attributable to hepatitis A.

**Recommendations for IG prophylaxis of hepatitis A.** Numerous field studies conducted in the past 4 decades confirm that IG given before exposure or during the incubation period of hepatitis A is protective against clinical illness (5-7). Its prophylactic value is greatest (80%-90%) when given early in the incubation period and declines thereafter (7).

**Preexposure prophylaxis.** The major group for whom preexposure prophylaxis is recommended is international travelers. The risk of hepatitis A for U.S. citizens traveling abroad varies with living conditions, incidence of hepatitis A infection in areas visited, and length of stay (8,9). In general, travelers to developed areas of western Europe, Japan, and Australia are at no greater risk of infection than in the United States. In contrast, travelers to developing countries may be at significant risk of infection. In such areas, the best way to prevent hepatitis A and other enteric diseases is to avoid potentially contaminated water or food. Drinking water (or beverages with ice) of unknown purity and eating uncooked shellfish or uncooked fruits or vegetables that are not peeled (or prepared) by the traveler should be avoided.

IG is recommended for travelers to developing countries if they will be eating in settings of poor or uncertain sanitation (some restaurants or homes) or will be visiting extensively with local persons, especially young children, in settings with poor sanitary conditions. Persons who plan to reside in developing areas for long periods should receive IG regularly if they anticipate exposure as described above or will be living in rural areas with poor sanitation.

For such travelers, a single dose of IG of 0.02 ml/kg is recommended if travel is for less than 2 months. For prolonged travel, 0.06 ml/kg should be given every 5 months. For persons who require repeated IG prophylaxis, screening for total anti-HAV antibodies before travel may be useful to define susceptibility and eliminate unnecessary doses of IG in those who are immune.

**Postexposure prophylaxis.** A serologic test for the diagnosis of acute hepatitis A is now widely available. Since only 38% of acute hepatitis cases in the United States result from hepatitis A, serologic confirmation of hepatitis A in the index case is recommended before treatment of contacts. Serologic screening of contacts for anti-HAV before giving IG is not recommended because screening is more costly than IG and would delay its administration.

IG should be given as soon as possible after exposure; giving IG more than 2 weeks after exposure is not indicated.

Specific recommendations for IG prophylaxis of hepatitis A depend on the nature of the HAV exposure:

1. *Close personal contact.* IG is recommended for all household and sexual contacts of persons with hepatitis A.
2. *Day-care centers.* Day-care facilities with children in diapers can be important settings for HAV transmission (10-12). IG should be administered to all staff and attendees of day-care centers or homes if: (a) one or more hepatitis A cases are recognized among children or employees; or (b) cases are recognized in two or more households of center attendees. When an outbreak (hepatitis cases in three or more families) occurs, IG should also be considered for members of households whose diapered children attend. In centers not enrolling children in diapers, IG need only be given to classroom contacts of an index case.
3. *Schools.* Contact at elementary and secondary schools is usually not an important means of transmitting hepatitis A. Routine administration of IG is not indicated for pupils and teachers in contact with a patient. However, when epidemiologic study clearly shows the existence of a school- or classroom-centered outbreak, IG may be given to those who have close personal contact with patients.
4. *Institutions for custodial care.* Living conditions in some institutions, such as prisons and facilities for the developmentally disabled, favor transmission of hepatitis A. When outbreaks occur, giving IG to residents and staff who have close contact with patients with hepatitis A may reduce the spread of disease. Depending on the epidemiologic circumstances, prophylaxis can be limited in extent or can involve the entire institution.
5. *Hospitals.* Routine IG prophylaxis for hospital personnel is not indicated. Rather, sound hygienic practices should be emphasized. Staff education should point out the risk of exposure to hepatitis A and emphasize precautions regarding direct contact with potentially infective materials (13).  
Outbreaks of hepatitis A among hospital staff occur occasionally, usually in association with an unsuspected index patient who is fecally incontinent. Large outbreaks have occurred among staff and family contacts of infected infants in neonatal intensive-care units. In outbreaks, prophylaxis of persons exposed to feces of infected patients may be indicated.
6. *Offices and factories.* Routine IG administration is not indicated under the usual office or factory conditions for persons exposed to a fellow worker with hepatitis A. Experience shows that casual contact in the work setting does not result in virus transmission.
7. *Common-source exposure.* IG might be effective in preventing foodborne or waterborne hepatitis A if exposure is recognized in time. However, IG is not recommended for persons exposed to a common source of hepatitis infection after cases have begun to occur in those exposed, since the 2-week period during which IG is effective will have been exceeded.

If a foodhandler is diagnosed as having hepatitis A, common-source transmission is possible but uncommon. IG should be administered to other foodhandlers but is usually not recommended for patrons. However, IG administration to patrons may be considered if (a) the infected person is directly involved in handling, without gloves, foods that will not be cooked before they are eaten; (b) the hygienic practices of the foodhandler are deficient; and (c) patrons can be identified and treated within 2 weeks of exposure. Situations where repeated exposures may have occurred, such as in institutional cafeterias, may warrant stronger consideration of IG use.

For postexposure IG prophylaxis, a single intramuscular dose of 0.02 ml/kg is recommended.

## HEPATITIS B

Hepatitis B virus (HBV) infection is a major cause of acute and chronic hepatitis, cirrhosis, and primary hepatocellular carcinoma worldwide. The frequency of HBV infection and patterns of transmission vary markedly in different parts of the world. In the United States, western Europe, and Australia, it is a disease of low endemicity, with only 0.1%-0.5% of the population being virus carriers and infection occurring primarily during adulthood. In contrast, HBV infection is highly endemic in China and Southeast Asia, sub-Saharan Africa, most Pacific islands, and the Amazon Basin; in these areas,

5%-15% of the population carry the virus, and most persons acquire infection at birth or during childhood. In other parts of the world, HBV is moderately endemic, and 1%-4% of persons are HBV carriers. Recommendations for prophylaxis of hepatitis B will vary in accordance with local patterns of HBV transmission. The recommendations that follow are intended for use in the United States.

Hepatitis B infection is caused by the HBV, a 42-nm, double-shelled deoxyribonucleic acid (DNA) virus. Several well-defined antigen-antibody systems have been associated with HBV infection (Table 1). HBsAg, formerly called "Australia antigen" or "hepatitis-associated antigen," is found on the surface of the virus and on accompanying 22-nm spherical and tubular forms. HBsAg can be identified in serum 30-60 days after exposure to HBV and persists for variable periods. The various subtypes (adr, adw, ayw, ayr) of HBsAg provide useful epidemiologic markers. Antibody against HBsAg (anti-HBs) develops after a resolved infection and is responsible for long-term immunity. Anti-HBc, the antibody to the core antigen (an internal component of the virus), develops in all HBV infections and persists indefinitely. IgM anti-HBc appears early in infection and persists for 6 or more months; it is a reliable marker of acute or recent HBV infection. The hepatitis B e antigen (HBeAg) is a third antigen, presence of which correlates with HBV replication and high infectivity. Antibody to HBeAg (anti-HBe) develops in most HBV infections and correlates with lower infectivity.

The onset of acute hepatitis B is generally insidious. Clinical symptoms and signs include various combinations of anorexia, malaise, nausea, vomiting, abdominal pain, and jaundice. Skin rashes, arthralgias, and arthritis can also occur. Overall fatality rates for reported cases generally do not exceed 2%. The incubation period of hepatitis B is long—45-160 days (average 60-120).

**HBV infection in the United States.** The estimated lifetime risk of HBV infection in the United States varies from almost 100% for the highest-risk groups to approximately 5% for the population as a whole. An estimated 200,000 persons, primarily young adults, are infected each year. One-quarter become ill with jaundice; more than 10,000 patients require hospitalization; and an average of 250 die of fulminant disease each year. Between 6% and 10% of young adults with HBV infection become carriers. The United States currently contains an estimated pool of 500,000-1,000,000 infectious carriers. Chronic active hepatitis develops in over 25% of carriers and often progresses to cirrhosis. Furthermore, HBV carriers have a risk of developing primary liver cancer that is 12-300 times higher than that of other persons. It is estimated that 4,000 persons die from hepatitis B-related cirrhosis each year in this country and that more than 800 die from hepatitis B-related liver cancer.

The role of the HBV carrier is central in the epidemiology of HBV transmission. A carrier is defined as a person who is HBsAg-positive on at least two occasions at least 6 months apart. Although the degree of infectivity is best correlated with HBeAg-positivity, any person positive for HBsAg is potentially infectious. The likelihood of developing the carrier state varies inversely with the age at which infection occurs. During the perinatal period, HBV transmitted from HBeAg-positive mothers results in HBV carriage in up to 90% of infected infants, whereas 6%-10% of acutely infected adults become carriers.

Carriers and persons with acute infection have highest concentrations of HBV in the blood and serous fluids; less is present in other body fluids, such as saliva and semen. Transmission occurs via percutaneous or permucosal routes. Infective blood or body fluids can be introduced by contaminated needles or through sexual contact. Infection can occur in settings of continuous close personal contact, such as in households or among children in institutions for the mentally retarded, presumably via inapparent or unnoticed contact of infectious secretions with skin lesions or mucosal surfaces. Transmission of infection by transfusion of contaminated blood or blood products has been greatly reduced since the advent of routine screening with highly sensitive tests for HBsAg. HBV is not transmitted via the fecal-oral route or by contamination of food or water.

Serologic surveys demonstrate that, although HBV infection is uncommon among adults in the general population, it is highly prevalent in certain groups. Those at risk, based on the prevalence of serologic markers of infection, are described in Table 2. Immigrants/refugees and their descendants from areas of high HBV endemicity are at high risk of acquiring HBV infection. Homosexually active men and users of illicit injectable drugs are among the highest-risk groups, acquiring infection soon after adopting these lifestyles (10%-20%/year). Inmates of prisons have high prevalence of HBV markers usually because of prior parenteral drug abuse; actual risk of transmission in prisons is also asso-

**TABLE 1. Hepatitis nomenclature**

| Abbreviation                           | Term   | Comments   |
|--|--|--|
| <b>Hepatitis A</b>                     |  |  |
| HAV                                    | Hepatitis A virus  | Etiologic agent of "infectious" hepatitis; a picornavirus; single serotype.  |
| Anti-HAV                               | Antibody to HAV  | Detectable at onset of symptoms; lifetime persistence.   |
| IgM anti-HAV                           | IgM class antibody to HAV  | Indicates recent infection with hepatitis A, positive up to 4-6 months after infection.                            |
| <b>Hepatitis B</b>                     |  |  |
| HBV                                    | Hepatitis B virus  | Etiologic agent of "serum" or "long-incubation" hepatitis, also known as Dane particle                             |
| HBsAg                                  | Hepatitis B surface antigen  | Surface antigen(s) of HBV detectable in large quantity in serum, several subtypes identified.                      |
| HBeAg                                  | Hepatitis B e antigen  | Soluble antigen; correlates with HBV replication, high titer HBV in serum, and infectivity of serum.               |
| HBcAg                                  | Hepatitis B core antigen   | No commercial test available.  |
| Anti-HBs                               | Antibody to HBsAg  | Indicates past infection with and immunity to HBV, passive antibody from HBIG, or immune response from HBV vaccine |
| Anti-HBe                               | Antibody to HBeAg  | Presence in serum of HBsAg carrier suggests lower titer of HBV.  |
| Anti-HBc                               | Antibody to HBcAg  | Indicates past infection with HBV at some undefined time   |
| IgM anti-HBc                           | IgM class antibody to HBcAg  | Indicates recent infection with HBV; positive for 4-6 months after infection.                                      |
| <b>Delta hepatitis</b>                 |  |  |
| $\delta$ virus                         | Delta virus  | Etiologic agent of delta hepatitis; may only cause infection in presence of HBV                                    |
| $\delta$ -Ag                           | Delta antigen  | Detectable in early acute delta infection.   |
| Anti- $\delta$                         | Antibody to delta antigen  | Indicates past or present infection with delta virus.  |
| <b>Non-A, non-B hepatitis</b>          |  |  |
| NANB                                   | Non-A, non-B hepatitis   | Diagnosis of exclusion. At least two candidate viruses; epidemiology parallels that of hepatitis B.                |
| <b>Epidemic non-A, non-B hepatitis</b> |  |  |
| Epidemic NANB                          | Epidemic non-A, non-B hepatitis  | Causes large epidemics in Asia, North Africa, fecal-oral or waterborne.  |
| <b>Immune globulins</b>                |  |  |
| IG                                     | Immune globulin (previously ISG, immune serum globulin, or gamma globulin) | Contains antibodies to HAV, low titer antibodies to HBV.   |
| HBIG                                   | Hepatitis B immune globulin  | Contains high titer antibodies to HBV.   |

ciated with parenteral drug abuse in prisons. Patients and staff in custodial institutions for the mentally retarded are also at increased risk of having HBV infection. Classroom contacts, particularly teachers or instructors, of some deinstitutionalized carriers may also be at higher risk than the general population. Household contacts and sexual partners of HBV carriers are at increased risk, as are hemodialysis patients and recipients of certain pooled plasma products.

There is increased risk for medical and dental workers and related laboratory and support personnel who have contact with blood. Employment in a hospital without exposure to blood carries no greater risk than that for the general population.

**Hepatitis B prophylaxis.** Two types of products are available for prophylaxis against hepatitis B. Hepatitis B vaccine, licensed in 1981, provides active immunization against HBV infection, and its use is recommended for both pre- and postexposure prophylaxis. IG products provide temporary, passive protection and are indicated only in certain postexposure settings.

**IG and HBIG.** IG and HBIG contain different amounts of anti-HBs. IG is prepared from plasma that is not preselected for anti-HBs content. Since 1977, all lots tested have contained anti-HBs at a titer of at least 1:100 by radioimmunoassay (RIA). HBIG is prepared from plasma preselected for high-titer anti-HBs. In the United States, HBIG has an anti-HBs titer of higher than 1:100,000 by RIA. There is no evidence that the causative agent of AIDS (HTLV-III/LAV) has been transmitted by IG or HBIG (4).

**Hepatitis B vaccine.** Hepatitis B vaccine licensed in the United States is a suspension of inactivated, alum-adsorbed 22-nm surface antigen particles that have been purified from human plasma by a combination of biophysical (ultracentrifugation) and biochemical procedures. Inactivation is a threefold process using 8M urea, pepsin at pH 2, and 1:4000 formalin. These treatment steps have been shown to inactivate representatives of all classes of viruses found in human blood, including the causative agent of AIDS (HTLV-III/LAV) (14). HB vaccine contains 20 µg/ml of HBsAg protein.

After a series of three intramuscular doses of hepatitis B vaccine, over 90% of healthy adults develop protective antibody (15,16). A course of three 10-µg doses induces antibody in virtually all infants and children from birth through 9 years of age. The deltoid (arm) is the recommended site for

**TABLE 2. Prevalence of hepatitis B serologic markers in various population groups**

| Population group                                      | Prevalence of serologic markers of HBV infection |                 |
|---|--|-----------------|
|   | HBsAg (%)  | All markers (%) |
| <b>High risk</b>                                      |  |                 |
| Immigrants/refugees from areas of high HBV endemicity | 13   | 70-85           |
| Clients in institutions for the mentally retarded     | 10-20  | 35-80           |
| Users of illicit parenteral drugs                     | 7  | 60-80           |
| Homosexually active men                               | 6  | 35-80           |
| Household contacts of HBV carriers                    | 3-6  | 30-60           |
| Patients of hemodialysis units                        | 3-10   | 20-80           |
| <b>Intermediate risk</b>                              |  |                 |
| Health-care workers—frequent blood contact            | 1-2  | 15-30           |
| Prisoners (male)                                      | 1-8  | 10-80           |
| Staff of institutions for the mentally retarded       | 1  | 10-25           |
| <b>Low risk</b>                                       |  |                 |
| Health-care workers—no or infrequent blood contact    | 0-3  | 3-10            |
| Healthy adults (first-time volunteer blood donors)    | 0-3  | 3-5             |



hepatitis B vaccination in adults; immunogenicity of vaccine in adults is significantly lower when injections are given in the buttock (81%) (17). The immunogenicity of the intradermal route has not yet been clearly established.

Field trials of the U.S.-manufactured vaccine have shown 80%-95% efficacy in preventing infection or hepatitis among susceptible persons (16,18). Protection against illness is virtually complete for persons who develop adequate antibody levels\* after vaccination. The duration of protection and need for booster doses are not yet defined. However, only 10%-15% of persons who develop adequate antibody after three vaccine doses will lose antibody within 4 years, and among those who lose antibody, protection against viremic infection and liver inflammation appears to persist. Immunogenicity and efficacy of the licensed vaccine in hemodialysis patients is much lower than in normal adults; protection may last only as long as adequate antibody levels persist (19).

**Vaccine usage.** Primary vaccination consists of three intramuscular doses of vaccine, with the second and third doses given 1 and 6 months, respectively, after the first. Adults and older children should be given 20  $\mu$ g (1.0 ml) per dose, while children under 10 years should receive 10  $\mu$ g (0.5 ml) per dose. For patients undergoing hemodialysis and for other immunosuppressed patients, a 40- $\mu$ g (2.0-ml) dose should be used. Vaccine doses administered at longer intervals provide equally satisfactory protection, but optimal protection is not conferred until after the third dose. Hepatitis B vaccine should only be given in the deltoid muscle in adults and children or in the anterolateral thigh muscle in infants and neonates. Since hepatitis B vaccine is an inactivated (noninfective) product, it is presumed that there will be no interference with other simultaneously administered vaccines.

Data are not available on the safety of the vaccine for the developing fetus. Because the vaccine contains only noninfectious HBsAg particles, there should be no risk to the fetus. In contrast, HBV infection in a pregnant woman may result in severe disease for the mother and chronic infection for the newborn. Pregnancy should not be considered a contraindication to the use of this vaccine for persons who are otherwise eligible.

**Vaccine storage.** Vaccine should be stored at 2 C-8 C (36 F-46 F) but not frozen. *Freezing destroys the potency of the vaccine.*

**Side effects and adverse reactions.** The most common side effect observed in prevaccination trials was soreness at the injection site. Among an estimated 750,000 vaccinees, approximately 100 episodes of severe illness have been reported after receipt of vaccine. These have included arthralgias, neurologic reactions (such as Guillain-Barré syndrome), and other illnesses. The rate of Guillain-Barré syndrome following HB vaccine does not appear to be significantly increased above that observed in normal adults. Such temporally associated illnesses are not considered to be etiologically related to hepatitis B vaccine.

**Effect of vaccination on carriers and immune persons.** The vaccine produces neither therapeutic nor adverse effects in HBV carriers (20). Vaccination of individuals who possess antibodies against HBV from a previous infection is not necessary but will not cause adverse effects. Such individuals will have a postvaccination increase in their anti-HBs levels. Passively acquired antibody, whether from HBIG or IG administration or from the transplacental route, will not interfere with active immunization (21).

**Prevaccination serologic screening for susceptibility.** The decision to screen potential vaccine recipients for prior infection depends on three variables: (1) the cost of vaccination; (2) the cost of testing for susceptibility; and (3) the expected prevalence of immune individuals in the group. Figure 1 shows the relative cost-effectiveness of screening, given different costs of screening tests and the expected prevalence of immunity. In constructing the figure, the assumption was made that the cost of three doses of vaccine is \$100 and that there are additional costs for administration. For any combination of screening costs and immunity to hepatitis, the cost-effectiveness can be estimated. For example, if the expected prevalence of serologic markers for HBV is over 20%, screening is cost-effective if costs of screening are no greater than \$30 per person. If the expected prevalence of markers is less than 8%, and if the costs of screening are greater than \$10 per person, vaccination without screening is cost-effective.

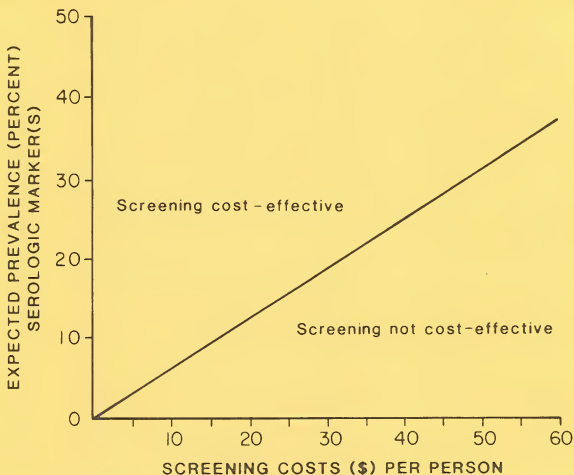
\*Adequate antibody is 10 or more sample ratio units (SRU) by RIA or positive by enzyme immunoassay.

Screening in groups with the highest risk of HBV infection (Table 2) will be cost-effective unless testing costs are extremely high. For groups at intermediate risk, cost-effectiveness of screening may be marginal, and vaccination programs may or may not utilize screening. For groups with a low expected prevalence of HBV serologic markers, such as health professionals in their training years, screening will not be cost-effective.

For routine screening, only one antibody test, either anti-HBc or anti-HBs, need be used. Anti-HBc will identify all previously infected persons, both carriers and noncarriers, but will not discriminate between members of the two groups. Anti-HBs will identify those previously infected, except carriers. For groups expected to have carrier rates of under 2%, such as health-care workers, neither test has a particular advantage. For groups with higher carrier rates, anti-HBc may be preferred to avoid unnecessary vaccination of carriers. If the RIA anti-HBs test is used for screening, a minimum of 10 RIA sample ratio units should be used to designate immunity (2.1 is the usual designation of a positive test). If enzyme immunoassay (EIA) is used, the manufacturers' recommended positive is appropriate.

**Serologic confirmation of postvaccination immunity and revaccination of nonresponders.** When given in the deltoid, hepatitis B vaccine produces protective antibody (anti-HBs) in more than 90% of healthy persons. Testing for immunity following vaccination is not recommended routinely but is advised for persons whose subsequent management depends on knowing their immune status, such as dialysis patients and staff, and for persons in whom a suboptimal response may be anticipated, such as those who have received vaccine in the buttock.

FIGURE 1. Cost-effectiveness of prevaccination screening of hepatitis B virus vaccine candidates\*



\*See text for assumptions.

Revaccination of persons who do not respond to primary series (nonresponders) produces adequate antibody in only one-third when the primary vaccination has been given in the deltoid. Therefore, revaccination of nonresponders to deltoid injection is not recommended routinely. For persons who did not respond to a primary vaccine series given in the buttock, preliminary data from two small studies suggest that revaccination in the arm induces adequate antibody in over 75%. Revaccination should be strongly considered for such persons.

**Preexposure vaccination.** Persons at substantial risk of acquiring HBV infection who are demonstrated or judged likely to be susceptible should be vaccinated. They include:

1. *Health-care workers.* The risk of health-care workers acquiring HBV infection depends on the frequency of exposure to blood or blood products and on the frequency of needlesticks. These risks vary during the training and working career of each individual but are often highest during the professional training period. For this reason, it is recommended that vaccination be completed during training in schools of medicine, dentistry, nursing, laboratory technology, and other allied health professions.

The risk of HBV infection for hospital personnel can vary both among hospitals and within hospitals. In developing specific immunization strategies, hospitals should use available published data about the risk of infection (22-24) and may wish to evaluate their own clinical and institutional experience with hepatitis B. Studies in urban centers have indicated that occupational groups with frequent exposure to blood and/or needles have the highest risk of acquiring HBV infection, including (but not limited to) the following groups: medical technologists, operating room staff, phlebotomists and intravenous therapy nurses, surgeons and pathologists, and oncology and dialysis unit staff. Groups shown to be at increased risk in some hospitals include: emergency room staff, nursing personnel, and staff physicians.

Other health-care workers based outside hospitals who have frequent contact with blood or blood products are also at increased risk of acquiring HBV infection. These include (but are not limited to): dental professionals (dentists, oral surgeons, dental hygienists), laboratory and blood bank technicians, dialysis center staff, emergency medical technicians, and morticians.

2. *Clients and staff of institutions for the mentally retarded.* Susceptible clients and staff who work closely with clients of institutions for the mentally retarded should be vaccinated. Risks for staff are comparable to those for health-care personnel in other high-risk environments. However, the risk in institutional environments is associated, not only with blood exposure, but also with bites and contact with skin lesions and other infective secretions. Susceptible clients and staff who live or work in smaller (group) residential settings with known HBV carriers should also receive hepatitis B vaccine.
3. *Hemodialysis patients.* Numerous studies have established the high risk of HBV transmission in hemodialysis units. Although recent data have shown not only a decrease in the rate of HBV infection in hemodialysis units but also a lower vaccine efficacy in these patients, vaccination is recommended for susceptible patients. Environmental control measures and regular serologic screening (based on immune status) of patients should be maintained.
4. *Homosexually active men.* Susceptible homosexually active men should be vaccinated regardless of their ages or duration of their homosexual practices. It is important to vaccinate persons as soon as possible after their homosexual activity begins. Homosexually active women are not at increased risk of sexually transmitted HBV infection.
5. *Users of illicit injectable drugs.* All users of illicit injectable drugs who are susceptible to HBV should be vaccinated as early as possible after their drug use begins.
6. *Recipients of certain blood products.* Patients with clotting disorders who receive clotting factor concentrates have an elevated risk of acquiring HBV infection. Vaccination is recommended for these persons and should be initiated at the time their specific clotting disorder is identified. Screening is recommended for patients who have already received multiple infusions of these products.
7. *Household and sexual contacts of HBV carriers.* Household contacts of HBV carriers are at high risk of acquiring HBV infection. Sexual contacts appear to be at greatest risk. When HBV carriers are identified through routine screening of donated blood, diagnostic testing in hospitals,

prenatal screening, screening of refugees, or other screening programs, they should be notified of their status and their susceptible household contacts vaccinated.

Families accepting orphans or unaccompanied minors from countries of high HBV endemicity should have the child screened for HBsAg, and if positive, family members should be vaccinated.

8. *Other contacts of HBV carriers.* Persons in casual contact with carriers at schools, offices, etc., are at minimal risk of acquiring HBV infection, and vaccine is not routinely recommended for them. However, classroom contacts of deinstitutionalized mentally retarded HBV carriers who behave aggressively or have special medical problems that increase the risk of exposure to their blood or serous secretions may be at risk. In such situations, vaccine may be offered to classroom contacts.
9. *Special high-risk populations.* Some American populations, such as Alaskan Eskimos, native Pacific islanders, and immigrants and refugees from areas with highly endemic disease (particularly eastern Asia and sub-Saharan Africa) have high HBV infection rates. Depending on specific epidemiologic and public health considerations, more extensive vaccination programs should be considered.
10. *Inmates of long-term correctional facilities.* The prison environment may provide a favorable setting for the transmission of HBV because of the frequent use of illicit injectable drugs and homosexual practices. Moreover, it provides an access point for vaccination of parenteral drug abusers. Prison officials should consider undertaking screening and vaccination programs directed at those who abuse drugs before or while in prison.
11. *Heterosexually active persons.* Heterosexually active persons with multiple sexual partners are at increased risk of acquiring HBV infection; risk increases with increasing sexual activity. Vaccination should be considered for persons who present for treatment of sexually transmitted diseases and who have histories of sexual activity with multiple partners.
12. *International travelers.* Vaccination should be considered for persons who plan to reside more than 6 months in areas with high levels of endemic HBV and who will have close contact with the local population. Vaccination should also be considered for short-term travelers who are likely to have contact with blood from or sexual contact with residents of areas with high levels of endemic disease. Hepatitis B vaccination of travelers ideally should begin 6 months before travel in order to complete the full vaccine series; however, a partial series will offer some protection against HBV infection.

**Postexposure prophylaxis for hepatitis B.** Prophylactic treatment to prevent hepatitis B infection after exposure to HBV should be considered in the following situations: perinatal exposure of an infant born to an HBsAg-positive mother; accidental percutaneous or permucosal exposure to HBsAg-positive blood; or sexual exposure to an HBsAg-positive person.

Recent studies have established the relative efficacies of immune globulins and/or hepatitis B vaccine in various exposure situations. For perinatal exposure to an HBsAg-positive, HBeAg-positive mother, a regimen combining one dose of HBIG at birth with the hepatitis B vaccine series started soon after birth is 85%-90% effective in preventing development of the HBV carrier state (25,27). Regimens involving either multiple doses of HBIG alone, or the vaccine series alone, have 70%-75% efficacy, while a single dose of HBIG alone has only 50% efficacy (28).

For accidental percutaneous exposure or sexual exposure, only regimens including HBIG and/or IG have been studied. A regimen of two HBIG doses, one given after exposure and one a month later, is about 75% effective in preventing hepatitis B following percutaneous exposure; a single dose of HBIG has similar efficacy when used following sexual exposure (29-31). IG may have some effect in preventing clinical hepatitis B following percutaneous exposures and can be considered as an alternative to HBIG when it is not possible to obtain HBIG.

Recommendations on postexposure prophylaxis are based on the efficacy data discussed above and on the likelihood of future HBV exposure of the person requiring treatment. In perinatal exposure and percutaneous exposure of high-risk health-care personnel, a regimen combining HBIG with hepatitis B vaccine will provide both short- and long-term protection, will be less costly than the two-dose HBIG treatment alone, and is the treatment of choice.

**Perinatal exposure.** One of the most efficient modes of HBV transmission is from mother to infant during birth. If the mother is positive for both HBsAg and HBeAg, about 70%-90% of infants will become infected, and up to 90% of these infected infants will become HBV carriers. If the HBsAg-positive carrier mother is HBeAg-negative, or if anti-HBe is present, transmission occurs less frequently and rarely leads to the HBV carrier state. However, severe acute disease, including fatal fulminant hepatitis in the neonate, has been reported (32,33). Prophylaxis of infants from all HBsAg-positive mothers is recommended, regardless of the mother's HBeAg or anti-HBe status.

The efficacy of a combination of HBIG plus the hepatitis B vaccine series has been confirmed in recent studies. Although the following regimen is recommended (Table 3), other schedules have also been effective (25-27,34). The major consideration for all these regimens is the need to give HBIG as soon as possible after delivery.

HBIG (0.5 ml [10 µg]) should be administered intramuscularly after physiologic stabilization of the infant and preferably within 12 hours of birth. Hepatitis B vaccine should be administered intramuscularly in three doses of 0.5 ml (10 µg) each. The first dose should be given concurrently with HBIG but at a different site. If vaccine is not available at birth, the first vaccine dose may be given within 7 days of birth. The second and third doses should be given 1 month and 6 months, respectively, after the first. Testing for HBsAg and anti-HBs is recommended at 12-15 months to monitor the final success or failure of therapy. If HBsAg is not detectable, and anti-HBs is present, the child has been protected. Testing for anti-HBc is not useful, since maternal anti-HBs may persist for more than 1 year; the utility of testing for IgM anti-HBc is currently being evaluated. HBIG administered at birth should not interfere with oral polio and diphtheria-tetanus-pertussis vaccines administered at 2 months of age.

**Maternal screening.** Since efficacy of the treatment regimen depends on administering HBIG on the day of birth, it is vital that HBsAg-positive mothers be identified before delivery. Mothers belonging to groups known to be at high risk of acquiring HBV infection (Table 4) should be tested routinely for HBsAg during a prenatal visit. If a mother belonging to a high-risk group has not been screened prenatally, HBsAg screening should be done at the time of delivery, or as soon as possible thereafter, and the infant treated as above if the mother is HBsAg-positive. If the mother is identified as HBsAg-positive more than 1 month after giving birth, the infant should be screened for HBsAg, and if negative, treated with hepatitis B vaccine and HBIG.

The appropriate obstetric and pediatric staff should be notified directly of HBsAg-positive mothers, so the staff may take appropriate precautions to protect themselves and other patients from infectious material, blood, and secretions, and so the neonate may receive therapy without delay after birth.

**Acute exposure to blood that contains (or might contain) HBsAg.** For accidental percutaneous or permucosal exposure to blood that is known to contain or might contain HBsAg, the decision to provide prophylaxis must take into account several factors: (1) the hepatitis B vaccination status of

**TABLE 3. Hepatitis B virus postexposure recommendations**

| Exposure  | HBIG          |  | Vaccine                    |   |
|-----------|---------------|--|----------------------------|---|
|           | Dose          | Recommended timing                           | Dose                       | Recommended timing                                  |
| Perinatal | 0.5 ml IM     | Within 12 hours                              | 0.5 ml (10 µg) IM of birth | Within 12 hours of birth*, repeat at 1 and 6 months |
| Sexual    | 0.06 ml/kg IM | Single dose within 14 days of sexual contact | †                          | —   |

\*The first dose can be given the same time as the HBIG dose but at a different site.

†Vaccine is recommended for homosexual men and for regular sexual contacts of HBV carriers and is optional in initial treatment of heterosexual contacts of persons with acute HBV.

the exposed person; (2) whether the source of blood is known or unknown; and (3) whether the HBsAg status of the source is known or unknown. Such exposures usually occur in persons who are candidates for hepatitis B vaccine; for any exposure in a person not previously vaccinated, hepatitis B vaccination is recommended.

The following outline and table summarize prophylaxis for percutaneous (needlestick or bite), ocular, or mucous-membrane exposure to blood according to the source of exposure and vaccination status of the exposed person (Table 5). For greatest effectiveness, passive prophylaxis with HBIG (or IG) should be given as soon as possible after exposure (its value beyond 7 days of exposure is unclear).

1. *Exposed person not previously vaccinated.* Hepatitis B vaccination should be considered the treatment of choice. Depending on the source of the exposure, HBsAg testing of the source and additional prophylaxis of the exposed person may be warranted (see below). Screening the exposed person for immunity should be considered if such screening is cost-effective (as discussed in preexposure prophylaxis) and if this will not delay treatment beyond 7 days.

**TABLE 4. Women for whom prenatal HBsAg screening is recommended**

- 1 Women of Asian, Pacific island, or Alaskan Eskimo descent, whether immigrant or U.S.-born.
- 2 Women born in Haiti or sub-Saharan Africa.
- 3 Women with histories of:
  - a Acute or chronic liver disease.
  - b Work or treatment in a hemodialysis unit.
  - c Work or residence in an institution for the mentally retarded.
  - d Rejection as a blood donor.
  - e Blood transfusion on repeated occasions.
  - f Frequent occupational exposure to blood in medico-dental settings.
  - g Household contact with an HBV carrier or hemodialysis patient.
  - h Multiple episodes of venereal diseases.
  - i Percutaneous use of illicit drugs.

**TABLE 5. Recommendations for hepatitis B prophylaxis following percutaneous exposure**

| Source                      | Exposed person  |   |
|-----------------------------|---|---|
|                             | Unvaccinated  | Vaccinated  |
| HBsAg-positive              | <ol style="list-style-type: none"> <li>1. HBIG x 1 immediately*</li> <li>2. Initiate HB vaccine† series.</li> </ol>                       | <ol style="list-style-type: none"> <li>1. Test exposed person for anti-HBs.§</li> <li>2. If inadequate antibody,¶ HBIG (x1) immediately plus HB vaccine booster dose.</li> </ol>                        |
| Known source                |   |   |
| High-risk<br>HBsAg-positive | <ol style="list-style-type: none"> <li>1. Initiate HB vaccine series</li> <li>2. Test source for HBsAg. If positive, HBIG x 1.</li> </ol> | <ol style="list-style-type: none"> <li>1. Test source for HBsAg only if exposed is vaccine nonresponder; if source is HBsAg-positive, give HBIG x 1 immediately plus HB vaccine booster dose</li> </ol> |
| Low-risk<br>HBsAg-positive  | Initiate HB vaccine series.   | Nothing required  |
| Unknown source              | Initiate HB vaccine series.   | Nothing required  |

\*HBIG dose 0.06 ml/kg IM.

†HB vaccine dose 20 µg IM for adults; 10 µg IM for infants or children under 10 years of age. First dose within 1 week; second and third doses, 1 and 6 months later.

§ See text for details.

¶ Less than 10 SRU by RIA, negative by EIA

- a. *Source known HBsAg-positive.* A single dose of HBIG (0.06 ml/kg) should be given as soon as possible after exposure and within 24 hours, if possible. The first dose of hepatitis B vaccine (20 µg) should be given intramuscularly at a separate site within 7 days of exposure, and the second and third doses given 1 month and 6 months later (Table 5).<sup>†</sup> If HBIG cannot be obtained, IG in an equivalent dosage (0.06 ml/kg) may provide some benefit.
  - b. *Source known, HBsAg status unknown.* The following guidelines are suggested based on the relative probability that the source is HBsAg-positive and on the consequent risk of HBV transmission:
    - (1) *High risk that the source is HBsAg-positive, such as patients with a high risk of HBV carriage (Table 2) or patients with acute or chronic liver disease (serologically undiagnosed).* The exposed person should be given the first dose of hepatitis B vaccine (20 µg) within 1 week of exposure and vaccination completed as recommended. The source person should be tested for HBsAg. If positive, the exposed person should be given HBIG (0.06 ml/kg) if within 7 days of exposure.
    - (2) *Low risk that the source is positive for HBsAg.* The exposed person should be given the first dose of hepatitis B vaccine (20 µg) within 1 week of exposure and vaccination completed as recommended. Testing of the source person is not necessary.
  - c. *Source unknown.* The exposed person should be given the first dose of hepatitis B vaccine (20 µg) within 7 days of exposure and vaccination completed as recommended.
2. *Exposed person previously vaccinated against hepatitis B.* For percutaneous exposures to blood in persons who have previously received one or more doses of hepatitis B vaccine, the decision to provide additional prophylaxis will depend on the source of exposure and on whether the vaccinated person has developed anti-HBs following vaccination.
- a. *Source known HBsAg-positive.* The exposed person should be tested for anti-HBs unless he/she has been tested within the last 12 months. If the exposed person has adequate<sup>§</sup> antibody, no additional treatment is indicated.
    - (1) If the exposed person has not completed vaccination and has inadequate levels of antibody, one dose of HBIG (0.06 ml/kg) should be given immediately and vaccination completed as scheduled.
    - (2) If the exposed person has inadequate antibody on testing or has previously not responded to vaccine, one dose of HBIG should be given immediately and a booster dose of vaccine (1 ml or 20 µg) given at a different site.
    - (3) If the exposed person shows inadequate antibody on testing but is known to have had adequate antibody in the past, a booster dose of hepatitis B vaccine (1 ml or 20 µg) should be given.
  - b. *Source known, HBsAg status unknown.*
    - (1) *High risk that the source is HBsAg-positive.* Additional prophylaxis is necessary only if the exposed person is a known vaccine nonresponder. In this circumstance, the source should be tested for HBsAg and, if positive, the exposed person treated with one dose of HBIG (0.06 ml/kg) immediately and a booster dose of vaccine (1 ml or 20 µg) at a different site. In other circumstances, screening of the source for HBsAg and the exposed person for anti-HBs is not routinely recommended, because the actual risk of HBV infection is very low (less than 1 per 1,000).<sup>¶</sup>
    - (2) *Low risk that the source is HBsAg-positive.* The risk of HBV infection is minimal. Neither testing of the source for HBsAg, nor testing of the exposed person for anti-HBs, is recommended.
  - c. *Source unknown.* The risk of HBV infection is minimal. No treatment is indicated.

<sup>†</sup>For persons who are not given hepatitis B vaccine, a second dose of HBIG should be given 1 month after the first dose.

<sup>§</sup>Adequate antibody is 10 SRU or more by RIA or positive by EIA.

<sup>¶</sup>Estimated by multiplying the risk of vaccine nonresponse in the exposed person (.10) by the risk of the needle source being HBsAg-positive (.05) by the risk of HBV infection in a susceptible person having an HBsAg-positive needle-stick injury (.20).

**Sexual contacts of persons with acute HBV infection.** Sexual contacts of HBsAg-positive persons are at increased risk of acquiring HBV infection, and HBIG has been shown to be 75% effective in preventing such infections (37). Because data are limited, the period after sexual exposure during which HBIG is effective is unknown, but extrapolation from other settings makes it unlikely that this period would exceed 14 days. Prescreening sexual partners for susceptibility before treatment is recommended if it does not delay treatment beyond 14 days after last exposure. Testing for anti-HBc is the most efficient prescreening test to use in this population group.

A single dose of HBIG (0.06 ml/kg) is recommended for susceptible individuals who have had sexual contact with an HBsAg-positive person, if HBIG can be given within 14 days of the last sexual contact, and for persons who will continue to have sexual contact with an individual with acute hepatitis B before loss of HBsAg in that individual. In exposures between heterosexuals, hepatitis B vaccination may be initiated at the same time as HBIG prophylaxis; such treatment may improve efficacy of postexposure treatment. However, since 90% of persons with acute HBV infection become HBsAg-negative within 15 weeks of diagnosis, the potential for repeated exposure to HBV is limited. Hepatitis B vaccine is, therefore, optional in initial treatment for such exposures. If vaccine is not given, a second dose of HBIG should be given if the index patient remains HBsAg-positive for 3 months after detection. If the index patient is a known carrier or remains positive for 6 months, hepatitis B vaccine should be offered to regular sexual contacts. For exposures among homosexual men, the hepatitis B vaccine series should be initiated at the time HBIG is given, since hepatitis B vaccine is recommended for all susceptible homosexual men. Additional doses of HBIG are unnecessary if vaccine is given. IG is an alternative to HBIG when it is not possible to obtain HBIG.

**Household contacts of persons with acute HBV infection.** Prophylaxis for other household contacts of persons with acute HBV infection is not indicated unless they have had identifiable blood exposure to the index case, such as by sharing toothbrushes or razors. Such exposures should be treated similarly to sexual exposures. If the index patient becomes a hepatitis B carrier, all household contacts should be given hepatitis B vaccine.

#### **DELTA HEPATITIS**

The delta virus (also known as hepatitis D virus [HDV] by some investigators) is a defective virus that may only cause infection in the presence of active HBV infection. The delta virus has been characterized as a particle of 35-37 nm in size, consisting of RNA (mw 500,000) as genetic material and an internal protein antigen (delta-antigen), coated with HBsAg as the surface protein (3). Infection may occur as either coinfection with hepatitis B or superinfection of a hepatitis B carrier, each of which usually cause an episode of acute hepatitis. Coinfection usually resolves, while superinfection frequently causes chronic delta infection and chronic active hepatitis. Both types of infection may cause fulminant hepatitis.

Delta infection may be diagnosed by detection of delta-antigen in serum during early infection and by the appearance of delta antibody during or after infection. Routes of delta transmission appear to be similar to those of hepatitis B. In the United States, delta infection occurs most commonly among persons at high risk of acquiring HBV infection, such as drug addicts and hemophilia patients.

A test for detection of delta antibody is expected to be commercially available soon. Other tests (delta antigen, IgM anti-delta) are available only in research laboratories.

Since the delta virus is dependent on hepatitis B for replication, prevention of hepatitis B infection, either preexposure or postexposure, will suffice to prevent delta infection in a person susceptible to hepatitis B. Known episodes of perinatal, sexual, or percutaneous exposure to sera or persons positive for both HBV and delta virus should be treated exactly as such exposures to hepatitis B alone.

Persons who are HBsAg carriers are at risk of delta infection, especially if they participate in activities that put them at high risk of repeated exposure to hepatitis B (parenteral drug abuse, homosexuality). However, at present there are no products available that might prevent delta infection in HBsAg carriers either before or after exposure.

#### **NON-A, NON-B HEPATITIS**

**United States.** Non-A, non-B hepatitis that presently occurs in the United States has epidemiologic characteristics similar to those of hepatitis B, occurring most commonly following blood transfusion and parenteral drug abuse. Multiple episodes of non-A, non-B hepatitis have been observed in



the same individuals and may be due to different agents. Chronic hepatitis following acute non-A, non-B hepatitis infection varies in frequency from 20% to 70%. Experimental studies in chimpanzees have confirmed the existence of a carrier state, which may be present in up to 8% of the population.

Although several studies have attempted to assess the value of prophylaxis with IG against non-A, non-B hepatitis, the results have been equivocal, and no specific recommendations can be made (35,36). However, for persons with percutaneous exposure to blood from a patient with non-A, non-B hepatitis, it may be reasonable to administer IG (0.06 ml/kg) as soon as possible after exposure.

**Epidemic (fecal-oral) non-A, non-B hepatitis.** In recent years, epidemics of non-A, non-B hepatitis spread by water or close personal contact have been reported from several areas of Southeast Asia (Indian subcontinent, Burma) and north Africa (2). Such epidemics generally affect adults and cause unusually high mortality in pregnant women. The disease has been transmitted to experimental animals, and candidate viruses have been identified; however, no serologic tests have yet been developed (37).

Epidemic non-A, non-B hepatitis has not been recognized in the United States or western Europe, and it is unknown whether the causative agent is present in these areas.

Travelers to areas having epidemic non-A, non-B hepatitis may be at some risk of acquiring this disease by close contact or by contaminated food or water. The value of IG in preventing this infection is unknown. The best prevention of infection is to avoid potentially contaminated food or water, as with hepatitis A and other enteric infections.

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Recommendations of the Immunization  
Practices Advisory Committee

**Update on Hepatitis B Prevention**

**INTRODUCTION**

Hepatitis B virus (HBV) infection is a major cause of acute and chronic hepatitis, cirrhosis, and primary hepatocellular carcinoma in the United States and worldwide. Since 1982, a safe and effective hepatitis B (HB) vaccine manufactured from human plasma has been available in the United States. This vaccine has been recommended as preexposure prophylaxis for persons at high or moderate risk of HBV infection (1). In addition, the combination of HB vaccine and hepatitis B immunoglobulin (HBIG) has been recommended for postexposure prophylaxis in susceptible persons who have perinatal or needle-stick exposure to known HBV-positive persons or their blood.

This statement provides an update on HB vaccine usage and on its impact on disease incidence in the 5 years following its licensure. In addition, it provides both recommendations for using a new HB vaccine produced in yeast by recombinant DNA technology and an assessment of the need for HB vaccine booster doses for persons who have received the initial three-dose regimen. Basic recommendations on preexposure and postexposure usage of HB vaccine and on prevaccination serologic testing for susceptibility to hepatitis B are unchanged. Previous recommendations should be consulted for a complete discussion of the usage of HB vaccine (1).

**PLASMA-DERIVED HB VACCINE**

**Patterns of Usage to Date**

Since the plasma-derived HB vaccine became available in June 1982, 4,400,000 doses have been distributed in the United States, and an estimated 1,400,000 persons have completed the three-dose series (Merck Sharp & Dohme, unpublished data). During this 5-year period, vaccination programs and overall vaccine usage have focused primarily on three risk groups—persons who work in health-care professions and have exposure to blood, staff and clients of institutions for the developmentally disabled, and staff and patients in hemodialysis units. Although no precise figures are available, it is estimated that more than 85% of distributed vaccine has been used for these groups.

Development of vaccination programs for health-care workers has progressed steadily since vaccine licensure. Several surveys of hospitals in 1985 showed that between 49% and 68% of hospitals had established HB vaccination programs and that the number has increased steadily each year (CDC, unpublished data). Large hospitals (>500 beds) were most likely to establish programs (90%). However, by June 1985, 60% of hospitals with fewer than 100 beds also had begun vaccination programs. In 75% of the programs, vaccination was recommended for high-risk health-care workers (as defined by the hospital), and, in 77%, the hospital paid for these vaccinations. In addition, 70% of states had established programs for vaccinating health-care workers under state jurisdiction (CDC, unpublished data).

In spite of these programs, the actual use of vaccine in high-risk health-care professions has been modest. One statewide survey showed that, in hospitals with HB vaccine programs, only 36% of persons at high risk had actually received vaccine (CDC, unpublished data). In one survey in three large cities, only 24% of physicians had received vaccine (CDC, unpublished data). National surveys have shown higher rates of vaccination among dentists (44% in early 1986) and hemodialysis staff (an estimated 44% in 1985); however, even these rates fall well short of optimal coverage (CDC, unpublished data).

Development of vaccination programs has also progressed for several other groups at high risk of HBV infection. By mid-1985, 94% of states had established vaccination programs for the developmentally disabled in institutions under state jurisdiction, and 75% had programs for staff of such facilities (CDC, unpublished data). By 1986, an estimated 27% of the developmentally disabled had received HB vaccine (Merck Sharp & Dohme, unpublished data). In addition, wide-scale programs directed at vaccinating all susceptible persons were established in 1981 for Alaskan Natives and in 1985 for the population of American Samoa.

Nevertheless, there has been little progress in developing vaccination programs for other major risk groups, including parenteral drug abusers, homosexual men, and heterosexually active persons with multiple sexual partners. Few states have established programs for offering vaccine to any of these groups, and private usage of vaccine among these groups is believed to be limited.

#### Impact on Disease Incidence

The incidence of reported hepatitis B has increased steadily over the last decade. Hepatitis B is now the most commonly reported type of hepatitis in the United States. In 1978, 15,000 cases of clinical hepatitis B were reported to CDC, for an incidence rate of 6.9/100,000 population. At that time, CDC estimated that there were actually 200,000 persons with HBV infection and that 50,000 of these had clinically confirmed cases with jaundice. The incidence rate of reported disease increased 33%, to 9.2/100,000, in 1981, the year prior to vaccine availability. It continued to increase during the initial 4 years of vaccine availability, reaching a rate of 11.5/100,000 in 1985 (2). Based on a comparison with the overall infection rate estimated in 1978, the incidence of HBV infection in the United States is now estimated at over 300,000 cases per year.

The apparent lack of impact of HB vaccine on the incidence of hepatitis B is attributable to several factors. First, the majority of acute hepatitis B cases now occur in three groups: homosexual men, parenteral drug abusers, and persons acquiring disease through heterosexual exposure (3). None of these groups is being reached effectively by current HB vaccine programs. In contrast, fewer than 10% of cases occur in health-care workers, the institutionalized developmentally disabled, and other groups currently accounting for the bulk of vaccine usage. Finally, up to 30% of patients deny any of the recognized risk factors, even after careful questioning. No effective strategy has been devised to prevent disease among this group, although some are probably undisclosed members of the three major risk groups.

A reduction in the incidence of hepatitis B can be expected only if significant proportions of persons at high risk receive vaccine. Increased efforts are needed to develop programs to vaccinate persons in all high-risk groups and to increase compliance among those who are susceptible in areas where programs are established. To have any effect on the incidence of hepatitis B, use of HB vaccine in the United States must extend beyond the current groups of recipients.

#### NEW RECOMBINANT DNA HB VACCINE

##### Formulation

In July 1986, a new, genetically engineered HB vaccine (Recombivax HB®; Merck Sharp & Dohme) was licensed by the U.S. Food and Drug Administration. This vaccine, as formulated, has an immunogenicity comparable to that of the currently available plasma-derived vaccine (Heptavax B®; Merck Sharp & Dohme). The two vaccines are also comparably effective when given with HBIG to prevent perinatal HBV transmission. The new vaccine provides an alternative to the plasma-derived HB vaccine for almost all groups at risk of HBV infection.

The recombinant vaccine is produced by *Saccharomyces cerevisiae* (common baker's yeast) into which a plasmid containing the gene for the Hepatitis B surface antigen (HBsAg) subtype adw has been inserted (4). HBsAg is harvested by lysing the yeast cells and is separated from yeast components by hydrophobic interaction and size-exclusion chromatography. The purified HBsAg protein undergoes sterile filtration and treatment with formalin prior to packaging. The vaccine is packaged to contain 10µg HBsAg protein per ml, adsorbed with 0.5 mg/ml aluminum hydroxide; a 1:20,000 concentration of thimerosal is added as a preservative.

The recombinant HBsAg takes the form of 17-25 nm spherical particles, similar in appearance to human plasma-derived HBsAg. The recombinant particles differ in that the HBsAg is not glycosylated, whereas up to 25% of plasma-derived HBsAg is glycosylated. The vaccine contains more than 95% HBsAg protein. Yeast-derived protein can constitute up to 4% of the final product, but no yeast DNA is detectable in the vaccine.

##### Immunogenicity and Efficacy

The immunogenicity of the recombinant HB vaccine is comparable to that of the plasma-derived product (5). When given in a three-dose series (10µg per dose), recombinant HB vaccine induces protective antibodies (anti-HBs\*) in over 95% of healthy adults 20-39 years of age. Studies comparing antibody responses of healthy adults show equal rates of seroconversion following the three doses of either the recombinant vaccine (10µg per dose) or the plasma-derived vaccine (20µg per dose). However, the geometric mean titers (GMT) of antibodies developed by recipients of the recombinant

\*Greater than 10 milli-International Units (mIU)/ml of anti-HBs, approximately equal to 10 sample ratio units by radioimmunoassay or positive by enzyme immunoassay.

vaccine have ranged from equal to 30% as high as those developed by recipients of the plasma-derived vaccine. The recombinant vaccine, like the plasma-derived vaccine, produces a somewhat lower antibody response in older adults than in younger adults (5).

In studies using three 5- $\mu$ g doses of recombinant vaccine for children <12 years of age, over 99% of the recipients have developed protective levels of antibodies. Hemodialysis patients develop a poorer response to the recombinant vaccine than do healthy adults. For example, in one study using three 40- $\mu$ g doses of recombinant HB vaccine, only 64% of vaccine recipients developed protective levels of antibodies.

The recombinant HB vaccine has been shown to prevent HBV infection of vaccinated chimpanzees challenged intravenously with HBV of either adw or ayr subtypes. In studies of infants born to HBsAg- and HBeAg-positive mothers, the combination of HBIG (0.5 cc at birth) and recombinant HB vaccine (5 $\mu$ g in each of three doses) protected 94% of infants from developing the chronic carrier state, an efficacy equalling that of HBIG plus plasma-derived HB vaccine (6). The simultaneous administration of HBIG did not interfere with induction of anti-HBs antibody response by the recombinant HB vaccine.

There have been no large-scale efficacy trials of recombinant vaccine in adults. Nevertheless, the immunogenicity studies, the challenge studies using chimpanzees, and the efficacy trials of the HB vaccine and HBIG in infants born to mothers who are carriers of HBV strongly suggest that the efficacy of recombinant HB vaccine in adults is comparable to that of the plasma-derived product.

#### **Safety**

Because only the portion of the HBV viral genome that codes for the surface coat of the virus (HBsAg) is present in the recombinant yeast cells, no potentially infectious viral DNA or complete viral particles can be produced. No human or animal plasma or other blood derivative is used in the preparation of recombinant HB vaccine.

During prelicensure trials, approximately 4,500 persons received at least one dose, and 2,700 persons completed the vaccine series (5). Reported side effects were similar in extent and variety to those following administration of the plasma-derived vaccine. Seventeen percent of those vaccinated experienced soreness at the injection site, and 15% experienced mild systemic symptoms (fever, headache, fatigue, and nausea). To date, no severe side effects have been observed, nor have significant allergic reactions been reported. Although yeast-derived proteins may constitute up to 4% of the protein in the vaccine, no adverse reactions that could be related to changes in titers of antibodies to yeast-derived antigens occurred during clinical trials.

Early concerns about safety of plasma-derived HB vaccine, especially the concern that infectious agents such as human immunodeficiency virus (HIV) present in donor plasma pools might contaminate the final product, have proven to be unfounded (7). There are no data to indicate that the recombinant vaccine is potentially or actually safer than the currently licensed plasma-derived product.

#### **Dosage and Schedule**

The recombinant HB vaccine is given in a series of three doses over a 6-month period. The second dose is administered 1 month after the first, and the third dose, 5 months after the second. For normal adults and children >10 years of age, the recommended dose is 10 $\mu$ g (1 ml) intramuscularly in each of the three inoculations. Children <11 years of age should receive a 5- $\mu$ g dose (0.5 ml) by the same schedule. Newborns of mothers who are carriers of HBsAg should receive the three-dose series (5 $\mu$ g per dose) by the same schedule; however, the first dose, which is given at birth, should be combined with a single dose of HBIG (0.5 ml) given intramuscularly at another site.

The recommended dose of recombinant HB vaccine for hemodialysis patients or other immunosuppressed persons is 40 $\mu$ g, which is identical to the dose of plasma-derived vaccine recommended for these groups. A specially formulated preparation (40 $\mu$ g HBsAg protein/ml adsorbed with 0.5 mg aluminum hydroxide) is being developed for these patients. At present, it is not advisable to administer the standard formulation of recombinant HB vaccine to these patients because this would require a large volume (4.0 cc), which is inconvenient for injection in the deltoid muscle, and would contain more aluminum hydroxide (2.0 mg) than currently recommended as an adjuvant in vaccines (1.25 mg per dose). Only plasma-derived vaccine should be used for these patients.

As with plasma-derived vaccine, recombinant HB vaccine should only be given to older children and adults in the deltoid muscle and to neonates or infants in the anterolateral thigh muscle. The vaccine should be stored at 2 C to 6 C (36 F to 43 F) and *should not be frozen*; freezing destroys the potency of this vaccine.

The response to vaccination by the standard schedule using one or two doses of plasma-derived vaccine followed by the remaining doses of recombinant vaccine has not been studied. However,

because the immunogenicities of the two vaccines are similar, it is likely that the response will be comparable to that induced by three doses of either vaccine alone. The response to revaccination with the recombinant vaccine following nonresponse to an initial series of plasma vaccine has not been evaluated.

#### Indications for Use

The indications for use of the recombinant HB vaccine are identical to those for the plasma-derived product, except that the present formulation of the recombinant HB vaccine should not be used for hemodialysis patients or other immunosuppressed persons (Table 1) (1). For other groups, including persons with Down's syndrome, there are no data indicating that the recombinant HB vaccine is either superior or inferior to the plasma-derived HB vaccine for any preexposure or postexposure indication.

#### Precautions

The recombinant HB vaccine contains only noninfectious HBsAg particles; therefore, vaccination of a pregnant woman should entail no risk to either the woman or the fetus. Furthermore, HBV infection in a pregnant woman can result in severe disease for the mother and chronic infection of the newborn. Pregnancy should not be considered a contraindication for women in high-risk groups who are eligible to receive this vaccine.

#### NEED FOR VACCINE BOOSTER DOSES

##### Long-Term Protection by Plasma-Derived HB Vaccine

In short-term efficacy studies, the plasma-derived HB vaccine provided protection against HBV infection for 85%-95% of vaccine recipients, including virtually all those who developed adequate levels of antibodies (see footnote on pg. 355) (8,9). A recent evaluation of the long-term protection afforded by this vaccine (>5 years) provides a basis for recommendations concerning the need for booster doses in previously vaccinated persons (10).

Currently available data indicate that vaccine-induced antibody levels decline significantly (10). Antibody may decrease to low levels for 30%-40% of vaccinated adults who initially develop adequate levels of antibody during the 5 years after vaccination, and it may become undetectable in 10%-15% of them. The duration of antibody persistence is directly related to the peak level achieved after the third dose of vaccine (11). The longer persistence of detectable levels of antibody observed in children and young adults (<20 years of age) is consistent with the higher peak response in these age groups.

Studies of the licensed plasma-derived HB vaccine in adults have demonstrated that, in spite of declining levels of antibody, protection against clinical (or viremic) HBV infection persists for >5 years (10). Although the risks of HBV infection appear to increase as antibody levels become low or undetectable, the resultant infections are almost always innocuous and do not cause detectable viremia, liver inflammation, or clinical illness. These infections are detected by serologic evidence of an increase of anti-HBs levels associated with the appearance of antibody to the hepatitis B core antigen (anti-HBc). To date, only one transient viremic infection has been recognized in a vaccine responder within 72 months after vaccination. This infection produced mild alanine aminotransferase elevation, but no clinical illness (10). Thus, among adults who have responded to the vaccine,

**TABLE 1. Persons for whom hepatitis B vaccine is recommended or should be considered\***

#### Preexposure

Persons for whom vaccine is recommended:

- Health-care workers having blood or needle-stick exposures
- Clients and staff of institutions for the developmentally disabled
- Hemodialysis patients
- Homosexually active men
- Users of illicit injectable drugs
- Recipients of certain blood products
- Household members and sexual contacts of HBV carriers
- Special high-risk populations

Persons for whom vaccine should be considered:

- Inmates of long-term correctional facilities
- Heterosexually active persons with multiple sexual partners
- International travelers to HBV endemic areas

#### Postexposure

- Infants born to HBV positive mothers
- Health-care workers having needle-stick exposures to human blood

\*Detailed information on recommendations for HB vaccination is available (1).

protection against clinically significant HBV infection appears to outlast the presence of detectable anti-HBs and can persist for >2 years among vaccine recipients whose antibodies have declined to low or undetectable levels.

For infants born to mothers who are carriers of HBV, there are insufficient data to assess duration of antibody persistence and protection against clinically significant HBV infection with the U.S. plasma-derived vaccine. One study, in a developing country (Senegal) and using a different plasma-derived HB vaccine, has demonstrated that protection against viremic HBV infection can decline within 6 years in infants vaccinated between 6 months and 2 years of age (12). Firm data on the duration of protection among infants receiving the vaccines licensed in the United States will be necessary before recommendations on booster doses can be made for this group.

#### **Postvaccination Testing of Response to Vaccine**

When properly administered, HB vaccine produces anti-HBs in more than 90% of healthy persons. Testing for immunity following vaccination has been recommended only for persons in whom suboptimal response to vaccine is anticipated, including persons who received vaccine in the buttock or persons, such as hemodialysis patients, whose subsequent management depends on knowing their immune

status (7). Revaccination, which has produced adequate antibody in only 30%-50% of persons who have not responded to primary vaccination in the deltoid, is not routinely recommended (1,10).

Vaccine program coordinators in hospitals may decide to test vaccine recipients serologically to assess their antibody responses, even though such postvaccination testing is not routinely recommended. Persons electing to do postvaccination testing should be aware of potential difficulties in interpreting the results. Serologic testing within 6 months of completing the primary series will differentiate persons who respond to vaccine from those who fail to respond. However, the results of testing undertaken more than 6 months after completion of the primary series are more difficult to interpret. A vaccine recipient who is negative for anti-HBs between 1 and 5 years after vaccination can be 1) a primary nonresponder who remains susceptible to hepatitis B or 2) a vaccine responder whose antibody levels have decreased below detectability but who is still protected against clinical HBV disease (10).

There is no need for routine anti-HBs testing 1 to 5 years after vaccination unless there has been a decision to provide booster doses for persons who are anti-HBs negative. This strategy is medically acceptable, but costly, and will prevent few additional cases of disease because of the excellent long-term protection already provided by the primary series of vaccine.

#### **Recommendations for Booster Doses**

*Adults and children with normal immune status.* For adults and children with normal immune status, the antibody response to properly administered vaccine is excellent, and protection lasts for at least 5 years. *Booster doses of vaccine are not routinely recommended, nor is routine serologic testing to assess antibody levels in vaccine recipients necessary during this period.* The possible need for booster doses after longer intervals will be assessed as additional information becomes available.

*Hemodialysis patients.* For hemodialysis patients, in whom vaccine-induced protection is less complete and may persist only as long as antibody levels remain above 10 mIU/ml, the need for booster doses should be assessed by semiannual antibody testing (13). Booster doses should be given when antibody levels decline below 10 mIU/ml.

#### **Postexposure Prophylaxis of Persons Exposed to HBsAg Positive Needle Sticks**

In vaccinated persons who experience percutaneous or needle exposure to HBsAg-positive blood, serologic testing to assess immune status is recommended unless testing within the previous 12 months has indicated adequate levels of antibody. If the exposed person is tested and found to have an inadequate antibody level, treatment with HBIG and/or a booster dose of vaccine is indicated, depending on whether vaccination has been completed and whether the person is known to have previously responded to HB vaccine. Detailed recommendations on prophylaxis in this situation are provided in the previous recommendations for HB vaccine (1).

#### **Dosage**

When indicated, HB vaccine recipients can be given booster doses of either plasma-derived or recombinant HB vaccine. Booster doses of either vaccine induce prompt anamnestic responses in over 90% of persons who initially respond to vaccine but subsequently lose detectable antibody (14,15). The booster dose for normal adults is 20µg of plasma-derived vaccine or 10µg of recombinant vaccine. For newborns and children <10 years of age, the dose is half that recommended for adults. For hemodialysis patients, a dose of 40µg of plasma-derived vaccine is recommended; a formulation of

recombinant HB vaccine is not yet available for this group. Vaccine should be given in the deltoid muscle. Buttock injection does not induce adequate levels of antibody.

#### Precautions:

Reported adverse effects following booster doses have been limited to soreness at the injection site. Data are not available on the safety of the vaccine for the developing fetus, but there should be no risk because both plasma-derived and recombinant HB vaccines are inactivated and do not contain live virus particles. Booster doses need not be withheld from pregnant women who are at ongoing risk of HBV infection.

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Recommendations of the Immunization  
Practices Advisory Committee

**Prevention of Perinatal Transmission of Hepatitis B Virus:  
Prenatal Screening of all Pregnant Women for Hepatitis B Surface Antigen**

Transmission of hepatitis B virus (HBV) from mother to infant during the perinatal period represents one of the most efficient modes of HBV infection and often leads to severe long-term sequelae. Infants born to mothers positive for hepatitis B surface antigen (HBsAg) and hepatitis B "e" antigen (HBeAg) have a 70%-90% chance of acquiring perinatal HBV infection, and 85%-90% of infected infants will become chronic HBV carriers (1,2). It has been estimated that more than 25% of these carriers will die from primary hepatocellular carcinoma or cirrhosis of the liver (3). These deaths usually occur during adulthood, when familial and financial responsibilities make them particularly devastating. In the United States, an estimated 16,500 births occur to HBsAg-positive women each year (about 4,300 of whom are also HBeAg-positive), and approximately 3,500 of these infants become chronic HBV carriers. Prenatal screening of all pregnant women would identify those who are HBsAg-positive and thus would allow treatment of their newborns with hepatitis B immune globulin (HBIG) and hepatitis B (HB) vaccine, a regimen that is 85%-95% effective in preventing the development of the HBV chronic carrier state (2,4-6).

In 1984, the Immunization Practices Advisory Committee (ACIP) recommended that pregnant women in certain groups at high risk for HBV infection be screened for HBsAg during a prenatal visit and, if found to be HBsAg-positive, that their newborns receive HBIG and HB vaccine at birth (7). No data are available regarding the proportion of high-risk women currently being screened in clinical practice, but several studies and the experience of public health workers indicate that major problems have been encountered in implementing these recommendations (8-12). These include 1) concerns about the sensitivity, specificity, and practicality of the current ACIP guidelines for identifying HBV carrier mothers; 2) lack of knowledge among prenatal health-care providers about the risks of perinatal transmission of HBV and about recommended screening and treatment procedures; 3) poor coordination among medical-care workers who provide treatment and follow-up of mothers and infants; and 4) refusal of some public and private third-party payers to reimburse for HBV screening of pregnant women and treatment of their infants. In addition, concern has been expressed that these recommendations may not be practical or applicable in some U.S. jurisdictions where HBV infection is highly endemic, such as parts of Alaska and certain Pacific Islands.

The problems encountered in implementing the currently recommended strategy of screening high-risk women have been examined by a number of investigators. Recent studies in several large inner-city hospitals, where all pregnant women were tested for HBsAg, have found that only about 35%-65% of HBsAg-positive mothers would have been identified by following the current ACIP guidelines (8-12). In these studies, the prevalence of HBsAg in inner-city black (0.4%-1.5%) and Hispanic women was higher than expected. Several investigators expressed concern that many health-care providers are too busy or may be reluctant to obtain the sexual and drug-use history necessary to identify high-risk patients for screening. In addition, persons providing health care to pregnant women often are not aware of the risks of perinatal transmission of HBV and of the recommended screening and treatment guidelines. In one study, 40% of obstetricians could name no more than two groups at high risk for HBV infection, and only 28% knew the recommended treatment for infants born to HBV carrier mothers (CDC, unpublished data).

Given these limitations, it is now evident that routine screening of all pregnant women is the only strategy that will provide acceptable control of perinatal transmission of HBV infection in the United States. Screening the approximately 3.5 million pregnant women per year for HBsAg would identify 16,500 positive women and allow treatment that would prevent about 3,500 infants from becoming

HBV carriers. Recent studies also indicate that the costs and benefits of universal testing of mothers are comparable to those encountered in other widely implemented programs of prenatal and blood-donor screening (13,14). The cost of an HBsAg test ranges from an estimated \$3.50 per test in blood-bank laboratories to \$21.00 per test in private commercial laboratories. If one assumes an average screening cost ranging from \$12.00 to \$20.00 per test plus \$150.00 for the HBIG and vaccine needed to treat each infant of an HBsAg-positive mother, the cost to prevent one newborn infant from becoming a chronic HBV carrier would be between \$12,700 and \$20,700.

HBsAg testing should be done early in pregnancy when other routine prenatal testing is done. The HBsAg test is widely available and can be added to the routine prenatal "panel" of tests without requiring additional patient visits. The advantages of making HBsAg testing routine during early pregnancy include 1) the ability to identify HBV carrier mothers that is not dependent on the health-care provider's identifying high-risk women or ordering HBsAg as a special test; 2) the availability of test results before delivery so that infants can receive HBIG and vaccine without delay after birth; and 3) appropriate counseling of families before delivery (15).

Because more than 90% of women found to be HBsAg-positive on routine screening will be HBV carriers, routine follow-up testing later in pregnancy is not necessary for the purpose of screening. In special situations, such as when the mother is thought to have acute hepatitis, when there has been a history of exposure to hepatitis, or when particularly high-risk behavior such as parenteral drug abuse has occurred during the pregnancy, an additional HBsAg test can be ordered during the third trimester. Few women in populations at low risk for HBV infection will have a change in HBsAg status during subsequent pregnancies. However, because of the expected benefits of making HBsAg testing a routine part of each prenatal panel, testing should be done during each pregnancy.

Women who present for delivery without prenatal care or without medical records documenting the results of HBsAg screening should have the HBsAg test done as soon as possible after admission, since delay in administration of HBIG to infants of carrier mothers will decrease the efficacy of therapy. In the studies that demonstrated the highest efficacy (85%–95%) of combined HBIG and HB vaccine prophylaxis, HBIG was administered within 2–12 hours after birth (2,4–6). In one study in which only HBIG was used for prophylaxis, no efficacy was found if HBIG was given more than 7 days after birth, and a significant decrease in efficacy was observed if it was given more than 48 hours after birth (16). Only one-third of U.S. hospitals currently perform the HBsAg test as an in-house procedure, and many of these have technicians who are trained to do the test available on only one shift. Hospitals that cannot rapidly test for HBsAg should either develop this capability or arrange for testing to be done at a local laboratory or blood bank where test results can be obtained within 24 hours.

The commercially available HBsAg tests have an extremely high sensitivity and specificity if positive tests are repeated and confirmed by neutralization as recommended by the manufacturers of the reagent kits. Testing for other markers of HBV infection, such as HBeAg, is not necessary for maternal screening. Mothers who are positive for both HBsAg and HBeAg have the highest likelihood of transmitting HBV to their newborns. However, infants of mothers who are HBsAg-positive but HBeAg-negative may become infected and develop severe, even fatal, fulminant hepatitis B during infancy (17,18). For this reason, HBIG and HB vaccine treatment of all babies born to HBsAg-positive women is recommended.

HBsAg-positive mothers identified during screening may have HBV-related acute or chronic liver disease and should be evaluated by a physician. Identification of women who are HBV carriers through prenatal screening presents an opportunity to vaccinate susceptible household members and sexual partners of HBV carriers, as previously recommended (19). Screening and vaccination of susceptible contacts should be done by the family's pediatrician, primary health-care provider, or the physician evaluating the clinical status of the HBsAg-positive pregnant women.

Implementation of the recommendations to prevent perinatal transmission requires maternal screening, treatment of the newborn in the hospital, and administration of subsequent doses of HB vaccine to the infant during pediatric visits at 1 and 6 months of age. This multistep process requires effective transfer of information among several groups of health-care providers, knowledge of recommended treatment, and availability of HBIG and vaccine at separate facilities. Treatment failures due to lack of communication among health-care providers can occur, especially in situations where prenatal, obstetric, and pediatric care are provided in different facilities (20). Central coordination of the treatment of these infants by city, county, or state health departments would improve the education of the health-care providers involved and increase the likelihood that proper treatment is provided.

In certain populations under U.S. jurisdiction, including Alaskan Natives and Pacific Islanders, as well as in many other parts of the world, HBV infection is highly endemic in the general population, and transmission occurs primarily during childhood (21). In such groups, universal vaccination of newborns with HB vaccine is recommended to prevent disease transmission both during the perinatal period and during childhood. Several studies have shown that HB vaccine given without HBIG will prevent 70%–85% of perinatal HBV infections and 95% of early childhood infections (22,23). In many of these areas with highly endemic HBV infection, prenatal screening is impractical because the population is isolated, laboratory facilities are not available, and/or health-care budgets and personnel are limited. In these areas, control of HBV infection can be better achieved by directing available resources into programs to vaccinate all children with HB vaccine. Programs for screening all mothers for HBsAg and providing HBIG to infants born to carrier mothers are costly and will add only modestly to disease prevention. They should be considered only after the program for universal vaccination of children has been implemented.

#### RECOMMENDATIONS

All pregnant women should be routinely tested for HBsAg during an early prenatal visit in each pregnancy. This testing should be done at the same time that other routine prenatal screening tests are ordered. In special situations, such as when acute hepatitis is suspected, when there has been a history of exposure to hepatitis, or when the mother has a particularly high-risk behavior such as intravenous drug abuse, an additional HBsAg test can be ordered later in the pregnancy.

If a woman has not been screened prenatally or if test results are not available at the time of admission for delivery, HBsAg testing should be done at the time of admission, or as soon as possible thereafter. If the mother is identified as HBsAg-positive more than 1 month after giving birth, the infant should first be tested for HBsAg; if negative, the infant should be treated with HBIG and HB vaccine. Hospitals where infants are delivered should have HBsAg testing capabilities or should be able to obtain HBsAg results within 24 hours from a local laboratory.

If a serum specimen is positive for HBsAg, the same specimen should be tested again, and then the test results should be confirmed by neutralization. It is unnecessary to test for other HBV markers during maternal screening, although HBsAg-positive mothers identified during screening may have HBV-related acute or chronic liver disease and should be evaluated by their physician.

Infants born to HBsAg-positive mothers should receive HBIG (0.5 mL) intramuscularly (IM) once they are physiologically stable, preferably within 12 hours after birth. HB vaccine, either plasma-derived (10 µg per dose) or recombinant (5 µg per dose), should be administered IM in three doses of 0.5 mL each. The first dose should be given concurrently with HBIG but at a different site. If vaccine is not immediately available, the first dose can be given within 7 days after birth. The second and third doses should be given 1 month and 6 months after the first. Testing the infant for HBsAg and its antibody (anti-HBs) is recommended at 12–15 months of age to monitor the effectiveness of therapy. If HBsAg is not detectable and anti-HBs is present, the child can be considered protected. Testing for antibody to hepatitis B core antigen (anti-HBc) is not useful, since maternal anti-HBc can persist for more than a year. HBIG and HB vaccination do not interfere with the routine childhood immunizations.

Household members and sexual partners of HBV carriers identified through prenatal screening should be tested to determine susceptibility to HBV infection and, if susceptible, should receive HB vaccine. Screening and vaccination of susceptible contacts should be done by the family's pediatrician, primary health-care provider, or the physician evaluating the clinical status of the HBsAg-positive pregnant women.

Obstetric and pediatric staff should be notified directly about HBsAg-positive mothers so that the neonate can receive therapy without delay after birth and follow-up doses of vaccine can be given. Hospitals, as well as state, county, and city health departments, should establish programs to educate appropriate health-care providers about perinatal transmission of HBV and its control through maternal screening, treatment of infants, and vaccination of susceptible household and sexual contacts of HBV carrier women.

Programs to coordinate the activities of those providing prenatal care, hospital-based obstetrical services, and pediatric well-baby care must be established to assure proper follow-up and treatment of infants born to HBsAg-positive mothers and other susceptible household and sexual contacts.

In populations under U.S. jurisdiction in which hepatitis B infection is highly endemic, including certain Alaskan Native and Pacific Island groups, vaccination of all newborns with HB vaccine is the most effective strategy for HB control. In these populations, such vaccination programs should be

given highest priority. In areas where HBsAg screening of mothers and use of HBIG in infants born to HBV carrier mothers are not practical, the vaccination of all newborns with HB vaccine should be considered the appropriate treatment.

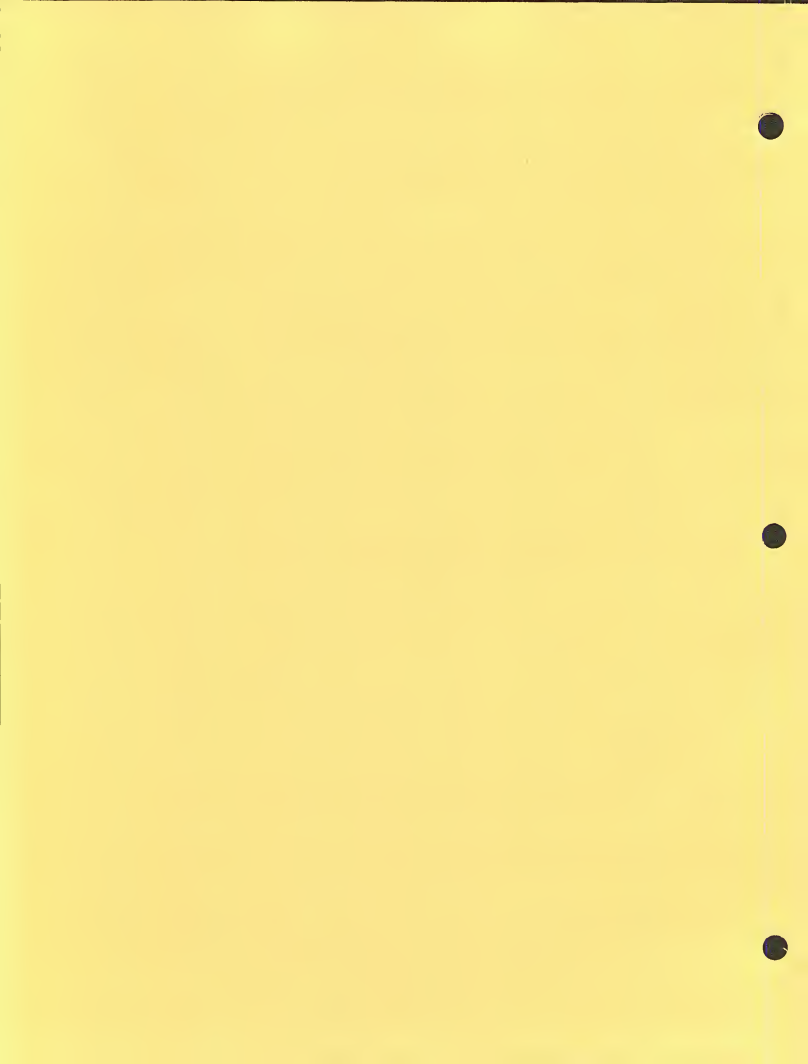
**Editorial Note:** Hepatitis B vaccine is the first human vaccine that can prevent both serious chronic disease and a uniformly fatal type of cancer. These recommendations, developed in consultation with representatives of the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics, represent a major step toward control of perinatal hepatitis B transmission in the United States. Programs for universal screening of pregnant women are currently in progress in Hawaii, certain Canadian provinces, Italy, West Germany, New Zealand, Australia, and Japan. More extensive infant HB vaccination programs are in progress in Alaska, American Samoa, Korea, Taiwan, Singapore, and the People's Republic of China. A number of U.S. health-care facilities have already begun to screen all pregnant women for HBsAg.

State and local health departments can facilitate implementation of these recommendations by 1) working to assure that all women receiving prenatal care in both public and private sector programs are offered screening and appropriate treatment; 2) working to assure that costs of screening and treatment are covered by public and private third-party payers; 3) establishing programs to coordinate the transfer of information between prenatal, obstetric, and pediatric health-care providers; and 4) providing health education about hepatitis B to the public and to health-care providers. CDC will continue to work with state and local health agencies and professional associations in hepatitis B prevention and control.

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# IMPORTANT INFORMATION ABOUT HEPATITIS B AND HEPATITIS B VACCINE

*Please Read This Carefully*

HEPATITIS B

4/1/86

## WHAT IS HEPATITIS B?

Hepatitis B is an infection of the liver caused by the hepatitis B virus (HBV). The term "viral hepatitis" is often used for and may include hepatitis B and other similar diseases which affect the liver but are caused by different viruses.

Acute hepatitis generally begins with mild symptoms that may or may not become severe. These symptoms may include loss of appetite, a vague feeling of oncoming illness, extreme tiredness, nausea, vomiting, stomach pain, dark urine, and jaundice (yellow eyes and skin). Skin rashes and joint pain can also occur.

In the United States about 200,000 persons, mostly young adults, catch hepatitis B each year. About 50,000 will develop jaundice, and about 10,000 will need to be hospitalized. About 250 people die each year from severe acute hepatitis B. Between 6 and 10 of every 100 young adults who catch hepatitis B become chronic carriers (have HBV in their blood for 6 or more months) and may be able to spread the infection to others for a long period of time. Infants who catch hepatitis B are more likely to become carriers than adults. About one-fourth of these carriers go on to develop a disease called "chronic active hepatitis." Chronic active hepatitis often causes cirrhosis of the liver (liver destruction) and death due to liver failure. In addition, HBV carriers are much more likely than others to get cancer of the liver. About 4,000 persons die from hepatitis B-related cirrhosis each year in the United States and more than 800 die from hepatitis B-related liver cancer.

The risk of catching hepatitis is higher in certain groups of people because of their occupation, lifestyle, or environment. Because of the risks of serious problems associated with hepatitis B infection, vaccination to help prevent infections is recommended for these groups.

**HEPATITIS B VACCINE:** Hepatitis B vaccine is made

*(PLEASE READ OTHER SIDE)*

from portions of HBV particles that have been purified from the blood of carriers. The methods used to prepare the vaccine kill all types of viruses found in human blood, including the virus that causes Acquired Immunodeficiency Syndrome (AIDS).

The vaccine is given by injection on three separate dates. The first two doses should be given 1 month apart, and the third dose, 5 months after the second. After three doses, the hepatitis B vaccine is 80%-95% effective in preventing hepatitis B infection in those who received vaccine. How long protection lasts after vaccination and the need for booster doses are not yet known.

**WHO SHOULD GET HEPATITIS B VACCINE?** The vaccine is recommended for persons at high risk of catching HBV infection who are or may be unprotected. These groups include:

1. **Health care workers.** The risk of health care workers catching HBV infection depends on how often they are exposed to blood or blood products and how often they get accidental needlesticks. Dental and laboratory workers are at especially high risk.
2. **Clients and staff of institutions for the mentally retarded.** The special behavioral and medical problems of the retarded make this a high risk setting. The risk in these institutions is related to contact with blood and also with bites and contact with skin lesions and other body fluids that contain HBV. Clients and staff of group and foster homes where a carrier is known to be present should also be vaccinated.
3. **Hemodialysis patients.** Although the hepatitis B vaccine is less effective in these patients, it should still be offered to all hemodialysis patients.

- 4 Homosexually active men
5. Use of unlawful injectable drugs. Sharing needles is an extremely high-risk activity for transmitting hepatitis B.
6. Recipients of certain blood products. Persons such as hemophiliacs who receive special products to help their blood clot are at high risk of infection.
7. Household and sexual contacts of HBV carriers. When HBV carriers are identified, household and sexual contacts should be offered vaccine.
8. Other contacts of HBV carriers. Persons who have casual contact with carriers at schools and offices are at little risk of catching HBV infection, and vaccine is not recommended for them. However, if mentally retarded HBV carriers behave aggressively or have special medical problems that may expose classroom contacts to their blood or body secretions, classroom contacts may be at risk and vaccine may be offered to them.
9. Special populations from areas with high rates of hepatitis B. These groups include Alaskan natives, native Pacific islanders, and immigrants and refugees from eastern Asia and sub-Saharan Africa.

**VACCINE ALSO SHOULD BE CONSIDERED FOR:**

10. Long-term inmates of prisons. The risks of prisoners catching HBV infection may be due to use of unlawful injectable drugs.
11. Heterosexuals who come in for treatment of sexually transmitted diseases and who have histories of sexual activity with multiple sexual partners.
12. Persons who plan to travel to areas outside the United States that have high rates of hepatitis B infection, stay in these areas for more than 6 months, and have close contact with the local population; and, persons traveling for shorter durations who may have sexual contact with local persons in areas where HBV infection is common. Persons traveling abroad who will perform medical procedures in areas where HBV infection is common are at very high risk.

**ADDITIONAL VACCINEES:** Hepatitis B vaccine is also

**PLEASE KEEP THIS PART OF THE INFORMATION SHEET FOR YOUR RECORDS**

*I have read the information on this form about hepatitis B and hepatitis B vaccine. I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and risks of the hepatitis B vaccine and request that it be given to me or to the person named below for whom I am authorized to make this request.*

**HEPATITIS B**  
4/1/86

| INFORMATION ABOUT PERSON TO RECEIVE VACCINE (Please Print)                      |            |       |           |      |
|---|------------|-------|-----------|------|
| Last Name   | First Name | MI    | Birthdate | Age  |
| Address   |            |       |           |      |
| City  | County     | State | Zip       |      |
| X   |            |       |           |      |
| Signature of person to receive vaccine or person authorized to make the request |            |       |           | Date |

| FOR CLINIC USE     |
|--------------------|
| Clinic Ident.      |
| Date Vaccinated    |
| Manuf. and Lot No. |
| Site of injection  |

**FOR DATA PROCESSING USE ONLY (OPTIONAL)**

| VACCINE HISTORY |        | PLACE CHECK | <input type="checkbox"/> | IN BOX IF HISTORY PREVIOUSLY SUBMITTED |        |          |                |
|-----------------|--------|-------------|--------------------------|--|--------|----------|----------------|
| DTP:            | m/d/yr | m/d/yr      | m/d/yr                   | m/d/yr                                 | m/d/yr | MEASLES: | MUMPS:         |
| POLIO:          | m/d/yr | m/d/yr      | m/d/yr                   | m/d/yr                                 | m/d/yr | RUBELLA: | HAEMOPHILUS b: |
|                 |        |             |                          |  |        |          | m/d/yr         |

recommended as part of the therapy used to prevent hepatitis B infection after exposure to HBV. Post exposure use of hepatitis B vaccine is recommended for the following persons: (1) infants born to mothers who have a positive blood test for hepatitis B surface antigen (HBsAg); and, (2) persons having accidents involving HBsAg-positive blood where there is entry through the skin or a mucous membrane. In addition, vaccination may be recommended for persons having sexual contact with someone who has a positive blood test for HBsAg. The hepatitis B vaccine series should be started at the same time as other therapy, primarily, treatment with hepatitis B immune globulin (HBIG).

**POSSIBLE SIDE EFFECTS FROM THE VACCINE:**

The most common side effect is soreness at the site of injection. Other illnesses, such as neurologic reactions, have been reported after vaccine is given but hepatitis B vaccine is not believed to be the cause of these illnesses. As with any drug or vaccine, there is a rare possibility that allergic or more serious reactions or even death could occur. No deaths, however, have occurred in over two million persons who have received this vaccine. Giving hepatitis B vaccine to persons who are already immune or to carriers will not increase the risk of side effects.

**PREGNANCY:** No information is available about the safety of the vaccine for unborn babies; however, because the vaccine contains only particles that do not cause hepatitis B infection, there should be no risk. In contrast, if a pregnant woman gets a hepatitis B infection, this may cause severe disease in the mother and chronic infection in the newborn baby. Therefore, pregnant women who are otherwise eligible can be given hepatitis B vaccine.

**QUESTIONS:** If you have any questions about hepatitis B or hepatitis B vaccine, please ask us now or call your doctor or health department before you sign this form.

**REACTIONS:** If the person who received the vaccine gets sick and visits a doctor, hospital, or clinic during the 4 weeks after receiving the vaccine, please report it to:



## Rabies

### VACCINE AVAILABILITY

The Montana Department of Health and Environmental Sciences supplies rabies vaccine (Human Diploid Cell - HDCV), pre- and post-exposure, and Rabies Immune globulin (RIG). Consultation related to possible rabies exposure is provided to help determine individual patient needs relating to treatment. The rabies treatments are purchased by the Department through a "revolving account" established by the state legislature. The rabies vaccine and RIG are provided at cost. The medical provider is charged for shipping and costs of the medication. The patient is not billed by DHES.

See following ACIP statement on rabies vaccine. Also, refer to the Adult Immunization Recommendation on Rabies and the Control of Communicable Diseases in Man.



## Rabies Prevention — United States, 1984

*These revised recommendations of the Immunization Practices Advisory Committee (ACIP) on rabies prevention update the previous recommendations (MMWR 1980, 29: 65-72, 277-80) to reflect the current status of rabies and antirabies biologics in the United States. For assistance on problems or questions about rabies prophylaxis, call local or state health departments.\**

### INTRODUCTION

Although rabies rarely affects humans in the United States, every year, approximately 25,000 persons receive rabies prophylaxis. Appropriate management of those who may have been exposed to rabies infection depends on the interpretation of the risk of infection and the efficacy and risk of prophylactic treatment. All available methods of systemic prophylactic treatment are complicated by instances of adverse reactions. These are rarely severe. Decisions on management must be made immediately; the longer treatment is postponed, the less likely it is to be effective.

Data on the efficacy of active and passive immunization after rabies exposure have come from both human and animal studies. Evidence from laboratory and field experience in many areas of the world indicates that postexposure prophylaxis combining local wound treatment, vaccine, and rabies immune globulin, is uniformly effective when appropriately used. However, rabies has occasionally developed in humans who had received postexposure antirabies prophylaxis with vaccine alone.

In the United States, rabies in humans has decreased from an average of 22 cases per year in 1946-1950 to zero to five cases per year since 1960. The number of rabies cases among domestic animals has decreased similarly. In 1946, more than 8,000 rabies cases were reported among dogs; 153 cases were reported in 1982. Thus, the likelihood of human exposure to rabies in domestic animals has decreased greatly, although bites by dogs and cats continue to be the principal reasons given for antirabies treatments.

The disease in wildlife—especially skunks, foxes, raccoons, and bats—has become more prevalent in recent years, accounting for approximately 85% of all reported cases of animal rabies every year since 1976. Wild animals now constitute the most important potential source of infection for both humans and domestic animals in the United States. Rabies among animals is present throughout the United States, only Hawaii remains consistently rabies-free.

Four of the six rabies fatalities in US citizens occurring between 1980 and 1983 were related to exposure to rabid dogs outside the United States. In much of the world, including most of Asia and all of Africa and Latin America, the dog remains the major source of human exposure.

### RABIES IMMUNIZING PRODUCTS

There are two types of immunizing products. (1) vaccines that induce an active immune response, which requires about 7-10 days to develop but may persist for as long as a year or more, and (2) globulins that provide rapid passive immune protection, which persists for a short period of time, with a half-life of about 21 days. Both types of products should be used concurrently for rabies postexposure prophylaxis.

#### Vaccines for Use in the United States

Human diploid cell rabies vaccine (HDCV)<sup>†</sup>: HDCV is an inactivated virus vaccine prepared from fixed rabies virus grown in WI-38 or MRC-5 human diploid cell culture. The vaccine grown on WI-38 cells and developed in the United States is inactivated with tri-n-butyl phosphate and  $\beta$ -propiolactone (Wyeth Laboratories' WYVAC<sup>®</sup>), while that grown in MRC-5 cells and developed in Europe is inactivated with  $\beta$ -propiolactone (Merieux Institute's RABIES VACCINE<sup>®</sup>). Both vaccines are supplied as 1.0 ml, single-dose vials of lyophilized vaccine with accompanying diluent.

#### Globulins

*Rabies Immune Globulin, Human (RIG)*: RIG (Cutter Laboratories' HYPERAB<sup>®</sup> and Merieux Institute's IMOGAM<sup>®</sup>) is antirabies gamma globulin concentrated by cold ethanol fractionation from plasma of hyperimmunized human donors. Rabies neutralizing antibody content is standardized to contain 150 international units (IU) per ml. It is supplied in 2-ml (300 IU) and 10-ml (1,500 IU) vials for pediatric and adult use, respectively.

*Antirabies Serum, Equine (ARS)*: ANTIRABIES SERUM<sup>®</sup> (Sclavo) is a refined, concentrated serum obtained from hyperimmunized horses. Neutralizing antibody content is standardized to contain 1,000 IU per vial. Volume is adjusted by the manufacturer on the basis of antibody potency in each lot. Currently, a 1,000-IU vial contains approximately 5 ml.

\*If these are unavailable, call the Division of Viral Diseases, Center for Infectious Diseases, CDC (404) 329-3095 during working hours, or (404) 329-2888 nights, weekends and holidays.

<sup>†</sup>Official name: Rabies Vaccine. The duck embryo vaccine which was used from 1957-1982 is no longer available in the United States.

## RATIONALE FOR CHOICE OF RABIES IMMUNIZING PRODUCTS

Both types of HDCV rabies vaccines are considered equally efficacious and safe when used as indicated on the labels. Only the Merieux Institute vaccine has been evaluated by the intradermal (ID) dose/route for preexposure immunization. No data are available on ID use with the Wyeth Laboratories vaccine. RIG is preferred over ARS, because the latter has a much higher risk of adverse reactions.

### Vaccines

The effectiveness of rabies vaccines is measured by their ability to protect persons exposed to rabies and to induce antibodies to rabies virus. HDCV has been used concurrently with RIG or ARS to treat 45 persons bitten by rabid dogs or wolves in Iran, 31 persons bitten by a variety of rabid animals in Germany, and 511 persons bitten by a variety of rabid animals in the United States. In these studies, no person contracted rabies after receiving HDCV in combination with RIG.

All persons treated with RIG and five 1.0-ml intramuscular (IM) doses of HDCV and tested have developed a rabies antibody titer. The definition of a minimally acceptable antibody titer varies between laboratories and is influenced by the type of test conducted. CDC currently specifies a 1:5 titer by the rapid fluorescent-focus inhibition test (RFFIT) as acceptable. The World Health Organization (WHO) specifies a titer of 0.5 I.U.

Serious adverse reactions associated with rabies vaccines include systemic, anaphylactic, and neuroparalytic reactions. Serious adverse reactions occur at lower rates in the HDCV vaccine than with previously available types of rabies vaccine.

### Globulins

RIG and ARS are both effective; however, ARS causes serum sickness in over 40% of adult recipients. RIG rarely causes adverse reactions and should be the product of choice when available.

## RATIONALE OF TREATMENT

Physicians must evaluate each possible rabies exposure. Local or state public health officials should be consulted if questions arise about the need for prophylaxis.

In the United States, the following factors should be considered before specific antirabies treatment is initiated:

### Species of Biting Animal

Carnivorous wild animals (especially skunks, raccoons, foxes, coyotes, and bobcats) and bats are the animals most commonly infected with rabies and have caused most of the indigenous cases of human rabies in the United States since 1960. Unless an animal is tested and shown not to be rabid, postexposure prophylaxis should be initiated upon bite or nonbite exposure to the animals. (See definition in "Type of Exposure" below.) If treatment has been initiated and subsequent testing in a competent laboratory shows the exposing animal is not rabid, treatment can be discontinued.

The likelihood that a domestic dog or cat is infected with rabies varies from region to region, hence, the need for postexposure prophylaxis also varies.

Rodents (such as squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, and mice) and lagomorphs (including rabbits and hares) are rarely found to be infected with rabies and have not been known to cause human rabies in the United States. In these cases, the state or local health department should be consulted before a decision is made to initiate postexposure antirabies prophylaxis.

### Circumstances of Biting Incident

An unprovoked attack is more likely than a provoked attack to indicate the animal is rabid. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as provoked.

### Type of Exposure

Rabies is transmitted by introducing the virus into open cuts or wounds in skin or via mucous membranes. The likelihood of rabies infection varies with the nature and extent of exposure. Two categories of exposure should be considered.

*Bite:* Any penetration of the skin by teeth.

*Nonbite:* Scratches, abrasions, open wounds, or mucous membranes contaminated with saliva or other potentially infectious material, such as brain tissue, from a rabid animal. Casual contact, such as petting a rabid animal (without a bite or nonbite exposure as described above), does not constitute an exposure and is not an indication for prophylaxis. There have been two instances of airborne rabies acquired in laboratories and two probable airborne rabies cases acquired in a bat-infested cave in Texas.

The only documented cases of rabies from human-to-human transmission occurred in four patients in the United States and overseas who received corneas transplanted from persons who died of rabies undiagnosed at the time of death. Stringent guidelines for acceptance of donor corneas should reduce this risk.

Bite and nonbite exposures from humans with rabies theoretically could transmit rabies, although no cases of rabies acquired this way have been documented. Each potential exposure to human rabies should be carefully evaluated to minimize unnecessary rabies prophylaxis.

## MANAGEMENT OF BITING ANIMALS

A healthy domestic dog or cat that bites a person should be confined and observed for 10 days and evaluated by a veterinarian at the first sign of illness during confinement or before release. Any illness in the animal should be reported immediately to the local health department. If signs suggestive of rabies develop, the animal should be humanely killed and its head removed and shipped, under refrigeration, for examination by a qualified laboratory designated by the local or state health department. Any stray or unwanted dog or cat that bites a person should be killed immediately and the head submitted, as described above, for rabies examination.

Signs of rabies in wild animals cannot be interpreted reliably, therefore, any wild animal that bites or scratches a person should be killed at once (without unnecessary damage to the head) and the brain submitted, as described above, for examination for evidence of rabies. If the brain is negative by fluorescent-antibody examination for rabies, the saliva can be assumed to contain no virus, and the bitten person need not be treated. If the biting animal is a particularly rare or valuable specimen and the risk of rabies small, consideration may be given to initiating postexposure treatment to the bitten person and delaying killing the animal for rabies testing.

### POSTEXPOSURE PROPHYLAXIS

The essential components of rabies postexposure prophylaxis are local treatment of wounds and immunization, including administration, in most instances, of both globulin and vaccine (Tables 1 and 2).

#### Local Treatment of Wounds

Immediate and thorough washing of all bite wounds and scratches with *soap and water* is perhaps the most effective measure for preventing rabies. In experimental animals, simple local wound cleansing has been shown to reduce markedly the likelihood of rabies.

Tetanus prophylaxis and measures to control bacterial infection should be given as indicated.

#### Immunization

Postexposure antirabies immunization should always include administration of both antibody (preferably RIG) and vaccine, with one exception: persons who have been previously immunized with the recommended preexposure or postexposure regimens with HDCV or who have been immunized with other types of vaccines and have a history of documented adequate rabies antibody titer (See "RATIONALE FOR CHOICE OF RABIES IMMUNIZING PRODUCTS") should receive only vaccine. The combination of globulin and vaccine is recommended for both bite exposures and nonbite exposures (as described under "RATIONALE OF TREATMENT"), regardless of the interval between exposure and treatment. The sooner treatment is begun after exposure, the better. However, there have been instances in which the decision to begin treatment was made as late as 6 months or longer after the exposure due to delay in recognition that an exposure had occurred.

**HDCV:** HDCV is the only type of vaccine currently available in the United States and should be administered in conjunction with RIG at the beginning of postexposure therapy, as described below. In 1977, WHO established a recommendation for six IM doses of HDCV based on studies in Germany and Iran of a regimen of RIG or ARS and six doses of HDCV. When used in this way, the vaccine was safe and effective in protecting 76 persons bitten by proven rabid animals. The vaccine also induced an excellent antibody response in all recipients. Studies conducted by CDC in the United States have shown that a regimen of one dose of RIG and five doses of HDCV was safe and induced an excellent antibody response in all recipients. Of 511 persons bitten by proven rabid animals and so treated, none developed rabies.

Five 1-ml doses of HDCV should be given intramuscularly (for example, in the deltoid region). Other routes of administration, such as the ID route, have not been adequately evaluated for postexposure prophylaxis and should not be used. The first dose should be given as soon as possible after exposure, an additional dose should be given on days 3, 7, 14 and 28 after the first dose (WHO currently recommends a sixth dose 90 days after the first dose.) Because the antibody response following the recommended vaccination regimen with HDCV has been so satisfactory, routine postvaccination serologic testing is not recommended in unusual instances, as when the patient is known to be immunosuppressed, serologic testing is indicated. Contact state health department or CDC for recommendations.

**RIG (or ARS if RIG is not available):** RIG is administered only once, at the beginning of antirabies prophylaxis, to provide immediate antibodies until the patient responds to HDCV by active production of antibodies. If RIG was not given when vaccination was begun, it can be given up to the eighth day after the first dose of vaccine was given. From about the eighth day on, RIG is not indicated, since an antibody response to the vaccine is presumed to have occurred. The recommended dose of RIG is 20 IU/kg or approximately 9 IU/lb of body weight (When ARS must be used, the recommended dose is 40 IU/kg, approximately 18 IU/lb or 1,000 IU/55 lb body weight.) If anatomically feasible, up to half the dose of RIG should be thoroughly infiltrated in the area around the wound, the rest should be administered intramus-

may suppress active production of antibody, no more than the recommended dose of RIG should be given.

TABLE 1. Rabies postexposure prophylaxis guide—July 1984

The following recommendations are only a guide. In applying them, take into account the animal species involved, the circumstances of the bite or other exposure, the vaccination status of the animal and presence of rabies in the region. Local or state public health officials should be consulted if questions arise about the need for rabies prophylaxis.

|          | Animal species   | Condition of animal at time of attack   | Treatment of exposed person*   |
|----------|--|---|--|
| DOMESTIC | Dog and cat  | Healthy and available for 10 days of observation  | None, unless animal develops rabies <sup>†</sup>   |
|          |  | Rabid or suspected rabid  | RIG <sup>‡</sup> and HDCV  |
|          |  | Unknown (escaped)   | Consult public health officials. If treatment is indicated, give RIG <sup>‡</sup> and HDCV |
| WILD     | Skunk, bat, fox, coyote, raccoon, bobcat, and other carnivores | Regard as rabid unless proven negative by laboratory tests <sup>§</sup>   | RIG <sup>‡</sup> and HDCV  |
| OTHER    | Livestock, rodents, and lagomorphs (rabbits and hares)         | Consider individually. Local and state public health officials should be consulted on questions about the need for rabies prophylaxis. Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other rodents, rabbits, and hares almost never call for antirabies prophylaxis. |  |

\*All bites and wounds should immediately be thoroughly cleansed with soap and water. If antirabies treatment is indicated, both rabies immune globulin (RIG) and human diploid cell rabies vaccine (HDCV) should be given as soon as possible, regardless of the interval from exposure. Local reactions to vaccines are common and do not contraindicate continuing treatment. Discontinue vaccine if fluorescent-antibody tests of the animal are negative.

<sup>†</sup>During the usual holding period of 10 days, begin treatment with RIG and HDCV at first sign of rabies in a dog or cat that has bitten someone. The symptomatic animal should be killed immediately and tested.

<sup>‡</sup>If RIG is not available, use antirabies serum, equine (ARS). Do not use more than the recommended dosage.

<sup>§</sup>The animal should be killed and tested as soon as possible. Holding for observation is not recommended.

TABLE 2. Rabies immunization—June 1984

I. PREEXPOSURE IMMUNIZATION. Preexposure immunization consists of three doses of HDCV, 1.0 ml, IM (i.e., deltoid area), one each on days 0, 7, and 28 (See text for details on use of 0.1 ml HDCV ID as an alternative dose/route.) Administration of routine booster doses of vaccine depends on exposure risk category as noted below. Preexposure immunization of immunosuppressed persons is not recommended.

| Criteria for Preexposure Immunization         |   |  |   |
|---|---|--|---|
| Risk category                                 | Nature of risk  | Typical populations  | Preexposure regimen   |
| Continuous                                    | Virus present continuously, often in high concentrations. Aerosol, mucous membrane, bite, or nonbite exposure possible. Specific exposures may go unrecognized. | Rabies research lab workers.*<br>Rabies biologics production workers.  | Primary preexposure immunization course.<br>Serology every 6 months.<br>Booster immunization when antibody titer falls below acceptable level. <sup>†</sup> |
| Frequent                                      | Exposure usually episodic, with source recognized, but exposure may also be unrecognized. Aerosol, mucous membrane, bite, or nonbite exposure.                  | Rabies diagnostic lab workers, <sup>‡</sup> spelunkers, veterinarians, and animal control and wildlife workers in rabies epizootic areas.                                | Primary preexposure immunization course.<br>Booster immunization or serology every 2 years <sup>†</sup>   |
| Infrequent (greater than population-at-large) | Exposure nearly always episodic with source recognized. Mucous membrane bite, or nonbite exposure.  | Veterinarians and animal control and wildlife workers in areas of low rabies endemicity.<br>Certain travelers to foreign rabies epizootic areas.<br>Veterinary students. | Primary preexposure immunization course.<br>No routine booster immunization or serology.  |
| Rare (population-at-large)                    | Exposure always episodic, mucous membrane, or bite with source recognized.  | U.S. population-at-large, including individuals in rabies-epizootic areas.   | No preexposure immunization.  |

TABLE 2. Rabies immunization — June 1984 — *Continued*

II. POSTEXPOSURE IMMUNIZATION. All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water

|   |  |
|---|--|
| Persons not previously immunized:           | RIG, 20 IU/kg body weight, one half infiltrated at bite site (if possible), remainder IM, 5 doses of HDCV, 1.0 ml IM (i.e., deltoid area), one each on days 0, 3, 7, 14 and 28 |
| Persons previously immunized <sup>§</sup> : | Two doses of HDCV, 1.0 ml, IM (i.e., deltoid area), one each on days 0 and 3. RIG should not be administered   |

\*Judgment of relative risk and extra monitoring of immunization status of laboratory workers is the responsibility of the laboratory supervisor (see U.S. Department of Health and Human Service's *Biosafety in Microbiological and Biomedical Laboratories*, 1984).

†Preexposure booster immunization consists of one dose of HDCV, 1.0 ml/dose, IM (deltoid area). Acceptable antibody level is 1:5 titer (complete inhibition in RFFIT at 1:5 dilution). Boost if titer falls below 1:5.

§Preexposure immunization with HDCV; prior postexposure prophylaxis with HDCV, or persons previously immunized with any other type of rabies vaccine and a documented history of positive antibody response to the prior vaccination.

#### TREATMENT OUTSIDE THE UNITED STATES

If postexposure is begun outside the United States with locally produced biologics, it may be desirable to provide additional treatment when the patient reaches the United States. State health departments should be contacted for specific advice in such cases.

#### PREEXPOSURE IMMUNIZATION

Preexposure immunization may be offered to persons in high-risk groups, such as veterinarians, animal handlers, certain laboratory workers, and persons spending time (e.g., 1 month or more) in foreign countries where rabies is a constant threat. Persons whose vocational or avocational pursuits bring them into contact with potentially rabid dogs, cats, foxes, skunks, bats, or other species at risk of having rabies should also be considered for preexposure prophylaxis.

Preexposure prophylaxis is given for several reasons. First, it may provide protection to persons with inapparent exposures to rabies. Second, it may protect persons whose postexposure therapy might be expected to be delayed. Finally, although it does not eliminate the need for additional therapy after a rabies exposure, it simplifies therapy by eliminating the need for globulin and decreasing the number of doses of vaccine needed. This is of particular importance for persons at high risk of being exposed in countries where the available rabies immunizing products may carry a higher risk of adverse reactions.

*Preexposure immunization does not eliminate the need for prompt postexposure prophylaxis following an exposure, it only reduces the postexposure regimen.*

#### Human Diploid Cell Rabies Vaccine

Three 1.0 ml injections of HDCV should be given intramuscularly (for example, in the deltoid area), one on each of days 0, 7, and 28. In a study in the United States, more than 1,000 persons received HDCV according to this regimen; antibody was demonstrated in the sera of all subjects when tested by the RFFIT. Other studies have produced comparable results. Because the antibody response following the recommended vaccination regimen with HDCV has been so satisfactory, routine postvaccination serology is not recommended.

#### Booster Doses of Vaccine

Persons who work with live rabies virus in research laboratories or vaccine production facilities and are at risk of inapparent exposure should have the rabies antibody titer of their serum determined every 6 months; booster doses of vaccine should be given, as needed, to maintain an adequate titer (See "RATIONALE FOR CHOICE OF RABIES IMMUNIZING PRODUCTS"). Other laboratory workers, such as those doing rabies diagnostic tests, spelunkers, and those veterinarians, animal control and wildlife officers in areas where animal rabies is epizootic should have boosters every 2 years or have their serum tested for rabies antibody every 2 years and, if the titer is inadequate, have a booster dose. Veterinarians and animal control and wildlife officers, if working in areas of low rabies endemicity, do not require routine booster doses of HDCV after completion of primary preexposure immunization (Table 2).

#### Postexposure Therapy of Previously Immunized Persons

When an immunized person who was vaccinated by the recommended regimen with HDCV or who had previously demonstrated rabies antibody is exposed to rabies, that person should receive two IM doses (1.0 ml each) of HDCV, one immediately and one 3 days later. RIG should not be given in these cases. If the immune status of a previously vaccinated person who did not receive the recommended HDCV regimen is not known, full primary postexposure

antirabies treatment (RIG plus five doses of HDCV) may be necessary. In such cases, if antibody can be demonstrated in a serum sample collected before vaccine is given, treatment can be discontinued after at least two doses of HDCV.

#### Intradermal Use of HDCV

HDCV produced by the Merieux Institute has been used for preexposure immunization in a regimen of three 0.1 ml doses given ID in the lateral aspect of the upper arm over the deltoid area, one dose each on days 0, 7, and 28. Experience gained with over 2,000 persons vaccinated in the United States by the ID route has shown that antibody was produced in all recipients, although the mean response was somewhat lower and may be of shorter duration than with comparable IM immunization. Antibody response in some groups vaccinated outside the United States has been found to be inadequate for reasons not yet determined.

Current data provide a sufficient basis to recommend the 0.1 ml ID dose/route as an alternative to the 1.0 ml IM dose/route for preexposure immunization in the United States. Postvaccination serology is not necessary following ID (or IM) immunization, except for persons suspected of being immunosuppressed. The manufacturer has not yet met the packaging and labeling requirements necessary to obtain approval by the U.S. Food and Drug Administration for the ID route. Since the 1.0-ml vial presently available is intended for IM use and contains no preservatives, the reconstituted vaccine must be used immediately. Data on ID immunization are not available for Wyeth Laboratories' vaccine, and it should not be used for ID vaccination.

#### ACCIDENTAL INOCULATION WITH MODIFIED LIVE RABIES VIRUS

Individuals may be accidentally exposed to attenuated rabies virus while administering modified live rabies virus (MLV) vaccines to animals. While there have been no reported human rabies cases resulting from exposure to needlesticks or sprays with licensed MLV vaccines, vaccine-induced rabies has been observed in animals given MLV vaccines. Absolute assurance of a lack of risk for humans, therefore, cannot be given. The best evidence for a low risk, however, is the absence of recognized cases of vaccine-associated disease in humans despite frequent accidental exposures.

Currently available MLV animal vaccines are made with one of two attenuated strains of rabies virus: high egg passage (HEP) Flury strain or Street Alabama Dufferin (SAD) strain. The HEP Flury and SAD virus strains have been used in animal vaccines for over 10 years without evidence of associated disease in humans; therefore, postexposure treatment is not recommended following exposure to these types of vaccine by needlesticks or sprays.

Because the data are insufficient to assess the true risk associated with any of the MLV vaccines, preexposure immunization, and periodic boosters are recommended for all persons dealing with potentially rabid animals or frequently handling animal rabies vaccines.

#### ADVERSE REACTIONS

##### Human Diploid Cell Rabies Vaccine

Reactions after vaccination with HDCV are less common than with previously available vaccines. In a study using five doses of HDCV, local reactions, such as pain, erythema, and swelling or itching at the injection site, were reported in about 25% of recipients of HDCV, and mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness were reported in about 20% of recipients. Two cases of neurologic illness resembling Guillain-Barré syndrome that resolved without sequelae in 12 weeks, and a focal subacute central nervous system disorder temporarily associated with HDCV vaccine, have been reported.

Recently, a significant increase has been noted in "immune complex-like" reactions in persons receiving booster doses of HDCV. The illness, characterized by onset 2-21 days post-booster, presents with a generalized urticaria and may also include arthralgia, arthritis, angioedema, nausea, vomiting, fever, and malaise. In no cases were the illnesses life-threatening. Preliminary data suggest this "immune complex-like" illness may occur in up to 6% of persons receiving booster vaccines and much less frequently in persons receiving primary immunization. Additional experience with this vaccine is needed to define more clearly the risk of these adverse reactions.

##### Vaccines in Other Countries

Many developing countries use inactivated nerve tissue vaccines (NTV) or inactivated suckling mouse brain vaccine (SMBV). NTV is reported to provoke neuroparalytic reactions at a rate of about 1/2,000 vaccinees, the rate for SMBV is about 1/8,000.

##### Rabies Immune Globulin, Human

Local pain and low-grade fever may follow receipt of RIG. Although not reported specifically for RIG, angioneurotic edema, nephrotic syndrome, and anaphylaxis have been reported after injection of immune serum globulin (ISG). These reactions occur so rarely that the causal relationship between ISG and these reactions is not clear.



#### Antirabies Serum, Equine

ARS produces serum sickness in at least 40% of adult recipients, reaction rates for children are lower. Anaphylactic reactions may occur. When RIG is not available, and ARS must be used, the patient should be tested for sensitivity to equine serum. (See package circular for details.)

Because adverse reactions are associated more frequently with ARS than with RIG, and ARS might sensitize recipients to equine protein, ARS should be used only when RIG cannot be obtained.

#### Management of Adverse Reactions

Once initiated, rabies prophylaxis should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine. Usually such reactions can be successfully managed with anti-inflammatory and antipyretic agents (aspirin, for example).

When a person with a history of hypersensitivity must be given rabies vaccines, antihistamines may be given; epinephrine should be readily available to counteract anaphylactic reactions, and the person should be carefully observed immediately after immunization.

Serious systemic anaphylactic or neuroparalytic reactions occurring during the administration of rabies vaccines pose a serious dilemma for the attending physician. A patient's risk of developing rabies must be carefully considered before deciding to discontinue vaccination. Moreover, the use of corticosteroids to treat life-threatening neuroparalytic reactions carries the risk of inhibiting the development of active immunity to rabies. It is especially important in these cases that the serum of the patient be tested for rabies antibodies. Advice and assistance on the management of serious adverse reactions in persons receiving rabies vaccines may be sought from the state health department or CDC.

All serious systemic neuroparalytic or anaphylactic reactions to a rabies vaccine should be immediately reported to the state health department or the Division of Viral Diseases, Center for Infectious Diseases, CDC ([404] 329-3095 during working hours, or [404] 329-2888 at other times).

#### PRECAUTIONS AND CONTRAINDICATIONS

##### Immunosuppression

Corticosteroids, other immunosuppressive agents, and immunosuppressive illnesses can interfere with the development of active immunity and predispose the patient to developing rabies. Immunosuppressive agents should not be administered during postexposure therapy, unless essential for the treatment of other conditions. When rabies postexposure prophylaxis is administered to persons receiving steroids or other immunosuppressive therapy, it is especially important that serum be tested for rabies antibody to ensure that an adequate response has developed.

##### Pregnancy

Because of the potential consequences of inadequately treated rabies exposure and limited data that indicate that fetal abnormalities have not been associated with rabies vaccination, pregnancy is not considered a contraindication to postexposure prophylaxis. If there is substantial risk of exposure to rabies, preexposure prophylaxis may also be indicated during pregnancy.

##### Allergies

Persons with histories of hypersensitivity should be given rabies vaccines with caution. When a patient with a history suggesting hypersensitivity to HDCV must be given that vaccine, antihistamines can be given; epinephrine should be readily available to counteract anaphylactic reactions, and the person should be carefully observed.

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Meningococcal

The Montana Immunization Program does not provide meningococcal vaccine. See the attached statement for Meningococcal vaccines and disease. Also, refer to the Adult Immunization Recommendation on Meningococcal disease and the Control of Communicable Diseases in Man.



## Meningococcal Vaccines

### INTRODUCTION

A polysaccharide vaccine against disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135 is currently licensed in the United States. This statement updates the previous statement (MMWR 1978;27:327-9), summarizes available information on the vaccine, and offers guidelines for its use in the civilian population of the United States.

### MENINGOCOCCAL DISEASE

*N. meningitidis* causes both endemic and epidemic disease, principally meningitis and meningococcemia. It is the second most common cause of bacterial meningitis in the United States (approximately 20% of all cases), affecting an estimated 3,000-4,000 people each year. The case-fatality rate is approximately 10% for meningococcal meningitis and 20% for meningococcemia, despite therapy with antimicrobial agents, such as penicillin, to which all strains remain highly sensitive.

No major epidemic of meningococcal disease has occurred in the United States since 1946, although localized community outbreaks have been reported. The incidence of endemic meningococcal disease peaks in the late winter to early spring. Attack rates are highest among children aged 6-12 months and then steadily decline; by age 5 years, the incidence approximates that for adults. Serogroup B, for which a vaccine is not yet available, accounts for 50%-55% of all cases; serogroup C, for 20%-25%; and serogroup W-135, for 15%. Serogroups Y (10%) and A (1%-2%) account for nearly all remaining cases. Serogroup W-135 has emerged as a major cause of disease only since 1975 (1). While serogroup A causes only a small proportion of endemic disease in the United States, it is the most common cause of epidemics elsewhere. Less commonly, serogroups C and B can also cause epidemic disease.

People with certain chronic conditions appear to be at increased risk of developing meningococcal infection. Meningococcal disease is particularly common among individuals with component deficiencies in the final common complement pathway (C3, C5-C9), many of whom experience multiple episodes of infection (2). Asplenic persons seem also to be at increased risk of developing meningococcal disease and experience particularly severe infections (3). It is uncertain whether individuals with other diseases associated with immunosuppression are at higher risk of acquiring meningococcal disease, as they are for disease caused by other encapsulated bacteria. In the past, new military recruits were at especially high risk, particularly for serogroup C disease; however, since routine vaccination of recruits with the bivalent A/C vaccine began in 1971, disease caused by those serogroups has been uncommon. Military recruits currently receive the A,C,Y,W-135 vaccine.

### MENINGOCOCCAL POLYSACCHARIDE VACCINES

The recently licensed quadrivalent A,C,Y,W-135 vaccine (Menomune<sup>®</sup>—A/C/Y/W-135, manufactured by Squibb-Connaught) is the formulation currently available in the United States. The vaccine consists of 50 µg each of the respective purified bacterial capsular polysaccharides.

**Vaccine efficacy.** Numerous studies have demonstrated the immunogenicity and clinical efficacy of the A and C vaccines. The serogroup A polysaccharide induces antibody in some children as young as 3 months of age, although a response comparable to that seen in adults is not achieved until 4 or 5 years of age; the serogroup C component does not induce a good antibody response before age 18-24 months (4,5). The serogroup A vaccine has been shown to have a clinical efficacy of 85%-95% and to be of use in controlling epidemics. A similar level of clinical efficacy has been demonstrated for the serogroup C vaccine, both in American military recruits and in an epidemic. The group Y and W-135 polysaccharides have been shown to be safe and immunogenic in adults (6-9) and in children over 2 years of age; clinical protection has not been demonstrated directly, but is assumed, based on the production of bactericidal antibody, which for group C has been correlated with clinical protection. The antibody responses to each of the four polysaccharides in the quadrivalent vaccine are serogroup-specific and independent.

**Duration of efficacy.** Antibodies against the group A and C polysaccharides decline markedly over the first 3 years following a single dose of vaccine (5,10-13). This antibody decline is more rapid in infants and young children than in adults. Similarly, while vaccine-induced clinical protection probably persists in schoolchildren and adults for at least 3 years, a recent study in Africa has demonstrated a marked decline in the efficacy of the group A vaccine in young children over time. In this study, efficacy declined from greater than 90% to less than 10% over 3 years in those under 4 years of age at the time of vaccination; in older children, efficacy was still 67% 3 years after vaccination (14).

#### RECOMMENDATIONS FOR VACCINE USE

Routine vaccination of civilians with meningococcal polysaccharide vaccine is not recommended for the following reasons: (1) the risk of infection in the United States is low; (2) a vaccine against serogroup B, the major cause of meningococcal disease in the United States, is not yet available; and (3) much of the meningococcal disease in the United States occurs among children too young to benefit from the vaccine. However, the vaccine has been shown to be of use in aborting outbreaks due to serogroups represented in the vaccine and should be used in their control. In an outbreak, the serogroup should be determined and the population at risk delineated by neighborhood, school, dormitory, or other reasonable boundary. Although endemic disease is very uncommon above age 5 years, older children, adolescents, and young adults constitute a higher proportion of cases during epidemics and may warrant vaccination during an outbreak (15).

Routine immunization with the quadrivalent vaccine is recommended for particular high-risk groups, including individuals with terminal complement component deficiencies and those with anatomic or functional asplenia. Persons splenectomized because of trauma or nonlymphoid tumors and those with inherited complement deficiencies have acceptable antibody responses to meningococcal vaccine, although clinical efficacy has not been documented (2,16). It should be recognized that such individuals frequently have preexisting antibody against *N. meningitidis* and may not be protected by vaccination.

Vaccination with the A-C vaccine may benefit some travelers to countries recognized as having hyperendemic or epidemic disease and Americans living in these areas, particularly those who will have prolonged contact with the local populace. One area of the world recognized as having recurrent epidemics of meningococcal disease is the part of sub-Saharan Africa known as the "meningitis belt," which extends from Mauritania in the west to Ethiopia in the east. Epidemics have been recognized in other parts of the world, and updated information can be obtained from travelers' clinics, state health departments, and CDC.

**Primary Immunization.** For both adults and children, vaccine is administered subcutaneously as a single 0.5-ml dose. The vaccine can be given at the same time as other immunizations, if needed. Good antibody levels are achieved within 10-14 days after vaccination.

#### PRECAUTIONS AND CONTRAINDICATIONS

**Reactions.** Adverse reactions to meningococcal vaccine are mild and infrequent, consisting principally of localized erythema lasting 1-2 days. Up to 2% of young children develop fever transiently after vaccination (13).

**Pregnancy.** On theoretical grounds, it is prudent not to immunize pregnant women unless there is a substantial risk of infection. However, evaluation of the vaccine in pregnant women during an epidemic in Brazil demonstrated no adverse effects. Further, antibody studies in these women showed good antibody levels in maternal and cord blood following vaccination during any trimester; antibody levels in the infants declined over the first few months and did not affect their subsequent response to immunization (17).

#### REVACCINATION

Revaccination may be indicated for individuals at high risk of infection, particularly children who were first immunized under 4 years of age; such children should be considered for revaccination after 2 or 3 years if they remain at high risk. The need for revaccination in older children and adults remains unknown.

## PROSPECTS FOR FUTURE MENINGOCOCCAL VACCINES

Work is continuing on a serogroup B meningococcal vaccine, as well as on improved A and C vaccines. Candidate vaccines include capsular polysaccharides complexed with meningococcal outer-membrane proteins or covalently linked to carrier proteins. Clinical efficacy data for these vaccines are not available.

## ANTIMICROBIAL CHEMOPROPHYLAXIS

Antimicrobial chemoprophylaxis of intimate contacts remains the chief preventive measure in sporadic cases of *N. meningitidis* disease in the United States. Intimate contacts include (1) household members, (2) day-care-center contacts, and (3) anyone directly exposed to the patient's oral secretions, such as through mouth-to-mouth resuscitation or kissing. The attack rate for household contacts is 0.3%-1%, 300-1,000 times the rate in the general population.

Unless the causative organism is known to be sensitive to sulfadiazine, the drug of choice is rifampin, given twice daily for 2 days (600 mg every 12 hours to adults; 10 mg/kg every 12 hours to children 1 month of age or older; 5 mg/kg every 12 hours to children under 1 month of age). Rifampin has been shown to be 90% effective in eradicating nasopharyngeal carriage. No serious adverse effects have been noted. However, rifampin prophylaxis is not recommended for pregnant women, as the drug is teratogenic in laboratory animals. Also, as well as turning urine orange, rifampin is excreted in tears, resulting in staining of contact lenses; thus, they should not be used during the course of therapy.

Because systemic antimicrobial therapy of meningococcal disease does not reliably eradicate nasopharyngeal carriage of *N. meningitidis*, it is also important to give chemoprophylaxis to the index patient before discharge from the hospital (18).

Nasopharyngeal cultures are not helpful in determining who warrants chemoprophylaxis and unnecessarily delay institution of this preventive measure.

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Chicken Pox - Herpes Zoster

As of this printing, there is no licensed vaccine for chicken pox although there is expected to be a licensed vaccine in the near future. See the attached ACIP statement on Varicella-Zoster Immune Globulin for the Prevention of Chickenpox. Also, refer to the Control of Communicable Diseases in Man.



Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Varicella-Zoster Immune Globulin for the Prevention of Chickenpox**

*This is the first statement by the Immunization Practices Advisory Committee (ACIP) on the use of varicella-zoster immune globulin (VZIG). Prior recommendations have been made by the manufacturer in cooperation with the Centers for Disease Control and approved by the Office of Biologics, National Center for Drugs and Biologics, U.S. Food and Drug Administration (FDA). Because of exceedingly limited supplies, VZIG use has been restricted to proven high-risk individuals—for prophylaxis against chickenpox in immunocompromised children and prevention of postnatal chickenpox following intrauterine exposure. With increasing supplies, some of these restrictions can be lifted. This statement includes use of VZIG for immunocompromised individuals of any age, normal adults, pregnant women, and premature and full-term infants. However, because the supply of VZIG is still limited, it continues to be recommended primarily for immunocompromised children and certain neonates exposed in utero. It should not be used indiscriminately.*

**INTRODUCTION**

Chickenpox or varicella is usually a benign, highly contagious disease caused by varicella-zoster (V-Z) virus. The disease occurs primarily among preschool and young, school-aged children. More than 90% of cases are reported among persons under 15 years of age. Epidemiologic and serologic studies confirm that susceptibility among adults is substantially lower than among children. Varicella is highly communicable; secondary clinical attack rates of about 90% follow exposure of household contacts (1). The period of communicability of patients with varicella is estimated to range from 1 to 2 days before rash onset through the first 5-6 days after rash onset. Persons with progressive varicella may be communicable for longer periods, presumably because their immune response is to some degree depressed, allowing viral replication to persist.

Because of the large number of varicella cases among normal children, children account for the greatest number of complications from this disease. However, the risk of complications for normal children is small compared to that for immunocompromised\* children, whose varicella can frequently be life-threatening. The risk of serious morbidity and mortality from varicella is directly related to host immunodeficiency.

Varicella can also be life-threatening to neonates who acquire infection transplacentally just before delivery. Term infants born to women who had onset of varicella rash within 4 days before delivery appear to have an increased mortality rate from varicella. Infants born to mothers with onsets of varicella rash 5 or more days before delivery usually have a benign course, presumably because of passive transfer of maternal antibody.

Although intrauterine infection acquired shortly before delivery increases the risk of neonatal complications, infection of mothers during the first 16 weeks of pregnancy only rarely leads to fetal damage (low birth weight, hypotrophic limbs, ocular abnormalities, brain damage, and mental retardation). This "syndrome" is so uncommon that two large studies of pregnancies complicated by varicella have not shown an increased incidence rate of congenital defects compared with controls (2,3). However, review of available case records clearly supports its existence.

Although few adults are susceptible to varicella, those who develop the disease are more likely to experience complications. Persons 20 years of age or older account for a disproportionate amount of encephalitis and death. Although less than 2% of reported cases occur among individuals 20 years of age or older, almost a quarter of all the mortality is reported in this age group. Pneumonia also appears to be more common among adults with varicella.

Following chickenpox, V-Z virus may persist in latent form without clinical manifestations. Upon reactivation, the latent virus can cause zoster or "shingles," a painful, vesicular, pustular eruption in the distribution of one or

\*Immunocompromised persons include individuals with congenital or acquired immunodeficiency diseases and persons with suppressed immune responses, such as those that occur with leukemia, lymphoma, generalized malignancy, end therapy with immunosuppressive drugs, including steroids, alkylating drugs, antimetabolites, or radiation.

more sensory-nerve roots. Zoster is more common among the elderly and among immunocompromised patients, who are also more prone than the general population to develop disseminated zoster with generalized skin eruptions and central nervous system, pulmonary, hepatic, and pancreatic involvement.

#### PREVENTION OF VARICELLA BY VARICELLA-ZOSTER IMMUNE GLOBULIN

In 1969, zoster immune globulin (ZIG), prepared from patients convalescing from herpes zoster, was shown to prevent clinical varicella in susceptible, normal children if administered within 72 hours after exposure. Subsequent uncontrolled studies of immunocompromised patients who received ZIG after exposure to V-Z virus showed that they also tended to have lower-than-expected clinical attack rates and higher-than-expected rates of subclinical infection when ZIG was administered no later than 96 hours after exposure. Patients who became ill tended to have modified illnesses with a low complication rate. The efficacy of ZIG in immunocompromised persons was further demonstrated by a study comparing the use of low-titer versus high-titer lots; patients who received the high-titer ZIG had significantly lower risks of complications.

In 1978, VZIG became available. Both serologic and clinical evaluations have demonstrated that the product is equivalent to ZIG in preventing or modifying clinical illness in susceptible, immunocompromised patients exposed to varicella. VZIG has been licensed by FDA's Office of Biologics. VZIG is prepared from plasma found in routine screening of normal, volunteer blood donors to contain high antibody titers to V-Z. VZIG (Human) is a sterile, 10%-18% solution of the globulin fraction of human plasma, primarily immunoglobulin G (IgG) in 0.3M glycine as a stabilizer and 1:10,000 thimerosol as a preservative. It is prepared by Cohn cold ethanol precipitation.

ZIG was in short supply because of the continuous need to find new donors convalescing from herpes zoster. Because of the method of routinely screening plasma from regular blood donors for high titers of V-Z antibody and using those units to prepare VZIG, supplies became substantially greater.

#### INDICATIONS FOR USE

When deciding whether to administer VZIG, the clinician must determine whether the patient is likely to be susceptible, whether the exposure is likely to result in infection, and whether the patient is at greater risk of complications from varicella than the general population. Whereas risks of VZIG administration appear to be negligible, costs of administration can be substantial (approximately \$75 per 125 units,<sup>†</sup> or \$375 for persons over 40 kg [88 lbs] of body weight, i.e., for the maximum recommended dose). In addition, it is not known whether modified infection will lead to lifelong immunity or whether modified infections will increase or decrease the risk of later developing zoster. The following recommendations are made taking these factors into account. In some instances, VZIG is routinely recommended; in others, administration should be evaluated on an individual basis.

##### Determination of Susceptibility

Both normal and immunocompromised adults and children, who are believed to have had varicella based on a carefully obtained history by an experienced interviewer, can be considered immune<sup>§</sup> (Table 1). Reports of second attacks of clinical varicella are rare.

Since subclinical primary infections appear rare (less than 5% of infections among normal children), children (under 15 years old) without histories of clinical varicella should be considered susceptible unless proven otherwise (see below). On the other hand, most normal adults with negative or unknown histories of varicella are probably immune, since attack rates of varicella in such adults after household or hospital exposure have ranged from only 5% to 15%.<sup>¶</sup>

**Antibody Assays:** Laboratory determination of susceptibility to varicella is often impractical. The most commonly available serologic assay for varicella antibodies, the complement-fixation (CF) test, is insensitive and may not be specific, particularly at low titers. One year after clinical varicella, approximately two of three patients will lack detectable CF antibody to varicella.

Other antibody assays are more sensitive and specific indicators of varicella immunity in normal hosts but are not generally available. These tests include fluorescent antibody against membrane antigen (FAMA), immune adherence hemagglutination (IAHA), enzyme-linked immunosorbent assay (ELISA), and neutralizing antibody. Commercial kits are available that utilize these sensitive antibody detection methods, although they have not been

<sup>†</sup>VZIG is, however, distributed free-of-charge to Massachusetts residents

<sup>§</sup>Except bone marrow recipients.

<sup>¶</sup>Susceptibility rates of adults who were raised in some tropical areas, such as Puerto Rico, and particularly remote areas may be somewhat higher

fully evaluated, particularly in immunocompromised populations.\*\* When sensitive tests are available, they can be used when a determination of susceptibility is necessary.

In some instances, there have been difficulties in interpreting results of some current sensitive antibody assays in immunocompromised persons. Low levels of such antibodies have been detected in the sera of some immunocompromised persons lacking histories of chickenpox who subsequently developed clinical varicella. While present, these antibodies did not prevent illness. Presumably, most if not all these persons had passively acquired antibodies as a result of recent transfusions of blood, blood derivatives, or blood products containing antibody. Investigation of other immunocompromised persons has demonstrated that serum antibodies are frequently present following transfusions. In addition, some of these sensitive antibody assays may be measuring nonspecific activity rather than antibody. Little is known about the cellular immune status of immunocompromised individuals. Therefore, until data are collected that allow further evaluation of serologic tests in the immunocompromised, in routine circumstances, one may need to rely primarily on a carefully obtained history of prior clinical chickenpox to define susceptibility. The history should be taken by an experienced interviewer. Additional studies to evaluate serologic tests of immunocompromised patients are in progress.

In addition, sensitive antibody assays may not be useful in assessing the likelihood that neonates and young infants exposed to varicella will develop clinical disease. Some infants have developed varicella after exposure, despite the presence of detectable antibody, although in most circumstances, such illnesses have been of modified severity.

**Bone Marrow Recipients:** Because data correlating a prior history of varicella in the bone marrow donor or recipient with actual immunity to chickenpox in the recipient are lacking, children or adults who have received bone marrow transplants should be considered susceptible, regardless of prior histories of clinical chickenpox either in themselves or in the transplant donor. However, bone marrow recipients who develop varicella or zoster following transplantation can subsequently be considered immune.

#### TYPES OF EXPOSURE

Several types of exposure are likely to place a susceptible person at risk for varicella (Table 2); persons continuously exposed in the household to patients with varicella are at greatest risk. Approximately 90% of such exposed, susceptible patients contract varicella after a single exposure. Data are not available from immunocompromised susceptible populations to directly compare the risk of varicella after playmate or hospital exposure with the risk after household exposure. However, clinical attack rates among immunocompromised patients

\*\*Some research laboratories have used experimental varicella skin-test antigens on a limited basis in selected populations, but their utility in routine screening programs has not been established.

TABLE 1. Determination of susceptibility to varicella in some selected situations\*

| Group                             | Immune status     | Carefully obtained prior history of varicella | Detectable varicella antibody by a reliable test <sup>†</sup> | Susceptibility status                    |
|-----------------------------------|-------------------|---|---|--|
| Children (< 15 yrs)               | immunocompromised | yes   | → unnecessary to perform                                      | → immune                                 |
|                                   |                   | no or unknown                                 | → §   | → susceptible                            |
| Adolescents and adults (≥ 15 yrs) | normal            | yes   | → unnecessary to perform                                      | → immune                                 |
|                                   |                   | no or unknown                                 | → not performed   | → generally consider immune <sup>‡</sup> |
|                                   |                   | yes   | →   | → immune                                 |
|                                   |                   | no  | →   | → susceptible                            |
|                                   | immunocompromised | yes   | → unnecessary to perform                                      | → immune                                 |
|                                   |                   | no or unknown                                 | → §   | → consider susceptible <sup>¶</sup>      |

\*This table provides general guidelines for determining susceptibility in frequently encountered situations. Not all potential scenarios are considered. In all situations, individual judgment should also be used. See text for details.

<sup>†</sup>Reliable tests are discussed in the text.

<sup>‡</sup>Some immunocompromised persons with detectable antibody before VZIG administration, presumably passively transferred by recent transfusions, have developed clinical varicella. Until further evaluation of serologic tests in the immunocompromised has been completed, one may have to rely on a carefully obtained clinical history by an experienced interviewer to determine susceptibility (i.e., the absence of a history of clinical varicella).

<sup>¶</sup>More than 85% and probably more than 95% of such persons are immune.

treated with VZIG allow some comparison; approximately one-third to one-half of VZIG-treated immunocompromised children with negative histories of prior varicella become ill after household exposure. The risks of disease following playmate and hospital exposure are approximately one-fifth the risk after household exposure. Significant playmate contact generally consists of longer than 1 hour of play indoors. Significant exposure for hospital contacts consists either of sharing the same two- to four-bed hospital room with an infectious patient or of prolonged, direct face-to-face contact with an infectious person (e.g., nurses or doctors who care for the patient). Transient contacts (e.g., x-ray technicians and maintenance personnel) are less likely to result in transmission than more prolonged contacts.

The clinical attack rate in VZIG-treated, normal infants who have been exposed in utero shortly before delivery is as high as 30%-40%, which is not substantially different from reported rates without VZIG. However, complications are much lower in VZIG-treated infants.

## RECOMMENDATIONS FOR USE OF VZIG

### Infants and Children

**Immunocompromised Children:** The most important use of VZIG is for passive immunization of susceptible, immunocompromised children after significant exposure to chickenpox or zoster (Table 3). This includes children with primary immune deficiency disorders and neoplastic diseases and children currently receiving immunosuppressive treatment.

**Newborns of Mothers with Varicella Shortly before Delivery:** VZIG is indicated for newborns of mothers who develop chickenpox within 5 days before and 48 hours after delivery. VZIG is probably not necessary for newborns whose mothers develop varicella more than 5 days before delivery, since those infants should be protected from complications of varicella by transplacentally-acquired maternal antibody. There is no evidence to suggest that infants born to mothers who develop varicella more than 48 hours after delivery are at increased risk of complications of disease.

**Postnatal Exposure of Newborn Infants:** Premature infants who have significant postnatal exposure should be evaluated on an individual basis. Most premature infants of 28 weeks' gestation or more will have

TABLE 2. Exposure criteria for which varicella-zoster immune globulin (VZIG) is indicated\*

|    |   |
|----|---|
| 1. | One of the following types of exposure to persons with chickenpox or zoster:  |
| a. | Continuous household contact.   |
| b. | Playmate contact (generally > 1 hour of play indoors).  |
| c. | Hospital contact (in same two- to four-bed room or adjacent beds in a large ward or prolonged face-to-face contact with an infectious staff member or patient). |
| d. | Newborn contact (newborn of mother who had onset of chickenpox 5 days or less before delivery or within 48 hours after delivery).                               |
|    | AND   |
| 2. | Time elapsed after exposure is such that VZIG can be administered within 96 hours but preferably sooner.  |

\*Patients should meet both criteria.

TABLE 3. Candidates for whom varicella-zoster immune globulin (VZIG) is indicated.\*

|    |   |
|----|---|
| 1. | Susceptible to varicella-zoster (see text and Table 1).   |
| 2. | Significant exposure (see Table 2).   |
| 3. | Age of < 15 years, with administration to immunocompromised adolescents and adults and to other older patients on an individual basis (see text). |
| 4. | One of the following underlying illnesses or conditions:  |
| a. | Leukemia or lymphoma.   |
| b. | Congenital or acquired immunodeficiency.  |
| c. | Immunosuppressive treatment.  |
| d. | Newborn of mother who had onset of chickenpox within 5 days before delivery or within 48 hours after delivery.                                    |
| e. | Premature infant ( $\geq$ 28 weeks' gestation) whose mother lacks a prior history of chickenpox.  |
| f. | Premature infants (< 28 weeks' gestation or $\leq$ 1,000 g) regardless of maternal history.   |

\*Patients should meet the four criteria for VZIG candidates.

transplacentally-acquired maternal antibodies and are protected from complications of disease if the mother is immune. The risk of complications of postnatally-acquired varicella in the premature infant is unknown. However, since their immune systems may be compromised, it seems prudent to administer VZIG to exposed premature infants whose mothers have negative or uncertain histories of varicella. Such infants should be considered at risk as long as they require continued hospital care. Exposed infants of less than 28 weeks' gestation or birth weight of 1,000 g or less probably should receive VZIG regardless of maternal history, because they may not yet have acquired transplacental maternal antibody.

Normal-term infants who develop varicella following postnatal exposure are not known to be at any greater risk from complications of chickenpox than older children. VZIG is not recommended for normal-term infants exposed postnatally even if their mothers do not have a prior history of varicella.

#### Adults

**Immunocompromised Adults:** The complication rate for immunocompromised adults who contract varicella is likely to be substantially greater than for normal adults. Most (85%-95%) immunocompromised adults with negative or unknown histories of prior varicella are likely to be immune. After careful evaluation, adults who are believed susceptible and who have had significant exposures should receive VZIG to prevent complications.

**Normal Adults:** Chickenpox can be severe in normal adults. Based on available epidemiologic and clinical data, normal adults who develop varicella have a ninefold to 25-fold greater risk of complications, including death, than normal children. The estimated risk of death following varicella in normal adults is 50/100,000, compared with an estimated 2/100,000 among normal children. The decision to administer VZIG to an adult should be evaluated on an individual basis. Approximately 85%-95% of adults with negative or uncertain histories of varicella will be immune. The objective is to modify rather than prevent illness in hopes of inducing lifelong immunity. The clinician should consider the patient's health status, type of exposure, and likelihood of previous infection when deciding whether to administer VZIG. Adults who are older siblings of large families and adults whose children have had varicella are probably immune. If sensitive laboratory screening tests for varicella are available, they might be used to determine susceptibility, if time permits. If, after careful evaluation, a normal adult with significant exposure to varicella is believed susceptible, VZIG may be administered. However, it should be noted that VZIG supplies are still limited and that the cost of VZIG is substantial (an adult dose costs \$375).

Indiscriminate use of VZIG in normal adults would quickly exhaust supplies and prevent prophylaxis of known high-risk individuals, such as immunocompromised children and high-risk neonates. Persons in the latter two groups who develop varicella have estimated death-to-case ratios of at least 7,000/100,000 and 31,000/100,000, respectively, compared with 50/100,000 for normal adults.

**Pregnant Women:** Pregnant women should be evaluated the same way as other adults. Some experts have recommended VZIG administration for pregnant women with negative or uncertain prior histories of varicella who are exposed in the first or second trimester to prevent congenital varicella syndrome or in the third trimester to prevent neonatal varicella. However, there is no evidence that administration of VZIG to a susceptible, pregnant woman will prevent viremia, fetal infection, or congenital varicella syndrome. Because most immunosuppressed persons who receive VZIG after a significant exposure develop modified clinical disease or subclinical infection, it is theoretically possible that VZIG may prevent or suppress clinical disease in the normal mother without preventing fetal infection and disease. In the absence of evidence that VZIG can prevent congenital varicella syndrome or neonatal varicella, the primary indication for VZIG in pregnant women is to prevent complications of varicella in a susceptible adult patient rather than to prevent intrauterine infection. Neonates born to mothers who develop varicella within the 5 days preceding or 48 hours after delivery should receive VZIG regardless of whether the mother received VZIG.

#### Hospital Settings

**Personnel:** After exposure, hospital personnel with negative or uncertain prior histories of chickenpox should be evaluated in the same manner as other adults. When deciding whether to give VZIG to exposed hospital personnel, types of exposure and histories of prior exposure to patients with varicella should be taken into account. If available, sensitive laboratory tests for determining susceptibility can be used to assess candidacy for VZIG and whether work restrictions are necessary during the incubation period.

#### Hospital Management of Varicella

Ideally, health-care personnel caring for patients with chickenpox or zoster should be immune to varicella. Proper control measures to prevent or control varicella outbreaks in hospitals should include strict isolation precautions,<sup>††</sup> cohorting of exposed patients,<sup>§§</sup> early discharge when possible, and the use of immune staff.<sup>¶¶</sup>

<sup>††</sup>Whenever possible, patients should be in a negative-pressure room.

<sup>§§</sup>Exposed persons can share a room.

<sup>¶¶</sup>Most studies indicate that almost all adults with prior histories of varicella are immune. Thus, staff with positive histories should be considered immune. Serologic screening may be useful in defining immunity of staff with negative or uncertain histories.

Potentially susceptible hospital personnel (Table 1) with significant exposure should not have direct patient contact from the 10th through the 21st day after exposure, if they do not develop varicella. This is the period during which chickenpox may occur. If they develop varicella, they should not have direct patient contact until all lesions have dried and crusted, generally 6 days after rash onset.\*\*

In general, the same control measures should apply regardless of whether potentially susceptible personnel or patients receive VZIG. Data on clinical attack rates and incubation periods of varicella following VZIG administration to normal adults are lacking. Studies of immunocompromised children with negative histories of previous varicella treated with VZIG, who have had intense exposures, such as in the household setting, demonstrate that approximately one-third to one-half will develop clinical varicella and could be infectious. Many of the remaining susceptibles develop subclinical infections that theoretically may be infectious. In addition, VZIG may prolong the average incubation period in immunocompromised patients from 14 to 18 days. The vast majority of cases occur within 28 days of exposure in immunocompromised, VZIG-treated patients. Because of the potential of a prolonged incubation period, personnel who receive VZIG should probably not work in patient areas for 10-28 days following exposure if no illness occurs.

## USE

### Administration

VZIG is of maximum benefit when administered as soon as possible after the presumed exposure but may be effective given as late as 96 hours after exposure. VZIG has not been evaluated more than 96 hours after initial exposure.

VZIG is not known to be useful in treating clinical varicella or zoster or in preventing disseminated zoster, and it is not recommended for such use. The duration of protection after VZIG administration is unknown, but it seems reasonable that protection should last for at least one half-life of immune globulin—approximately 3<sup>†††</sup> weeks. To be safe, high-risk susceptibles who are again exposed more than 3 weeks after a prior dose of VZIG should receive another full dose.

### Dosage

VZIG is supplied in vials containing 125 units per vial (volume is approximately 1.25 cc). The recommended dose is 125 units per 10 kg (22 lbs) body weight, up to a maximum of 625 units (i.e., five vials). The minimum dose is 125 units. Fractional doses are not recommended. Some experts recommend 125 units per 10 kg of body weight without limiting the total dose to 625 units. VZIG has not been evaluated as a prophylactic measure for prevention or attenuation of varicella in normal or immunocompromised adults. Therefore, data do not exist with which to calculate the appropriate dose in adults. However, it seems likely that 625 units should be sufficient to prevent or modify infection in normal adults. Higher doses may be needed in immunocompromised adults.

### Route

VZIG should be administered intramuscularly as directed by the manufacturer. IT SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

### Supply

VZIG is produced by the Massachusetts Public Health Biologic Laboratories. Outside Massachusetts, distribution is arranged by the American Red Cross Blood Services—Northeast Region, through other centers (Table 4). VZIG is distributed within Massachusetts by the Massachusetts Public Health Biologic Laboratories.

## ADVERSE REACTIONS AND PRECAUTIONS

The most frequent adverse event following VZIG is local discomfort at the injection site. Pain, redness, or swelling occurs at the injection site in about 1% of patients. Less frequent adverse reactions are gastrointestinal symptoms, malaise, headache, rash, and respiratory symptoms that occur in approximately 0.2% of recipients. Severe reactions, such as angioneurotic edema and anaphylactic shock, are rare (less than 0.1%).

When VZIG is indicated for patients with severe thrombocytopenia or any other coagulation disorder that would ordinarily contraindicate intramuscular injections, the expected benefits should outweigh the risks.

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\*\*It should be remembered that staff with varicella may be contagious 1-2 days before onset of rash.

†††In the absence of increased loss or turnover of immunoglobulin (e.g., nephrotic syndrome or Wiskott-Aldrich syndrome).



**TABLE 4. Varicella-zoster immune globulin regional distribution centers**

| Service area              | Regional center and 24-hour telephone  | Service area  | Regional center and 24-hour telephone  |
|---------------------------|--|---|--|
| Massachusetts             | Massachusetts Public Health<br>Biologics Laboratories<br>305 South St.<br>Jamaica Plain, MA 02130<br>(617) 522-3700  | or  | American Red Cross<br>Blood Services<br>Rochester Region<br>50 Prince St.<br>Rochester, NY 14607<br>(716) 461-9800                               |
| Maine                     | American Red Cross<br>Blood Services<br>Northeast Region<br>812 Huntington Ave.<br>Boston, MA 02115<br>(617) 731-2130  | or  | American Red Cross<br>Blood Services<br>Syracuse Region<br>636 S. Warren St.<br>Syracuse, NY 13202<br>(315) 425-1647                             |
| or                        | American Red Cross<br>Blood Services<br>Northeast Region-<br>Portland Location<br>524 Forest Ave.<br>Portland, ME 04101<br>(207) 775-2367  | Delaware,<br>Pennsylvania,<br>Southern<br>New Jersey      | American Red Cross<br>8lood Services<br>Penn-Jersey Region<br>23rd and Chestnut<br>Philadelphia, PA 19103<br>(215) 299-4110                      |
| Connecticut               | American Red Cross<br>Blood Services<br>Connecticut Region<br>209 Farmington Ave.<br>Farmington, CT 06032<br>(203) 678-2730  | Maryland  | American Red Cross<br>Blood Services<br>Baltimore Region<br>2701 N. Charles St.<br>Baltimore, MD 21218<br>(301) 467-9905                         |
| Vermont,<br>New Hampshire | American Red Cross<br>Blood Services<br>Vermont-New Hampshire<br>Region<br>32 N. Prospect St.<br>Burlington, VT 05402<br>(802) 658-6400  | Virginia  | American Red Cross<br>Blood Services<br>Tidewater Region<br>611 W. Brambleton Ave.<br>P.O. Box 1836<br>Norfolk, VA 23501<br>(804) 446-7708       |
| Rhode Island              | Rhode Island Blood Center<br>551 N. Main St.<br>Providence, RI 02904<br>(401) 863-8368   | or  | Richmond Metropolitan<br>Blood Service<br>2201 Westwood Ave.<br>Richmond, VA 23230<br>(804) 359-5100   |
| New Jersey,<br>New York   | The Greater New York<br>Blood Program<br>150 Amsterdam Ave.<br>New York, NY 10023<br>(212) 570-3067<br>(212) 570-3068 (night)  | Washington, D.C.,<br>Maryland, Virginia,<br>West Virginia | American Red Cross<br>Blood Services<br>Washington Region<br>2025 E Street, N.W.<br>Washington, DC 20006<br>(202) 728-6426                       |
| New York                  | American Red Cross<br>Blood Services<br>Northeastern New York Region<br>Hockett Blvd. at<br>Clara Barton Dr.<br>Albany, NY 12208<br>(518) 449-5020<br>(518) 462-7461<br>(518) 462-6964 (night) | Georgia   | American Red Cross<br>Blood Services<br>Atlanta Region<br>1925 Monroe Dr., N.E.<br>Atlanta, GA 30324<br>(404) BB1-9800<br>(404) 881-6752 (night) |
| or                        | American Red Cross<br>Blood Services<br>Greater Buffalo Chapter<br>786 Delaware Ave.<br>Buffalo, NY 14209<br>(716) 886-7500  | North Carolina  | American Red Cross<br>Blood Services<br>Carolinas Region<br>2425 Park Rd.<br>Charlotte, NC 28236<br>(704) 376-1661                               |

**TABLE 4. Varicella-zoster immune globulin regional distribution centers — Continued**

| Service area            | Regional center and 24-hour telephone  | Service area   | Regional center and 24-hour telephone   |
|-------------------------|--|--|---|
| South Carolina          | American Red Cross<br>Blood Services<br>South Carolina Region<br>1100 Shirley St.<br>Columbia, SC 29205<br>(803) 256-2301                    | or   | American Red Cross<br>Central Ohio Region<br>995 E. Broad St.<br>Columbus, OH 43205<br>(614) 253-7981   |
| Florida                 | South Florida<br>Blood Service<br>1675 N.W. Ninth Ave.<br>Miami, FL 33136<br>(305) 326-8888  | Wisconsin, Iowa,<br>North Dakota,<br>South Dakota                | The Blood Center of<br>S.E. Wisconsin<br>1701 W. Wisconsin Ave.<br>Milwaukee, WI 53233<br>(414) 933-5000  |
| or                      | American Red Cross<br>Blood Services<br>Mid-Florida Region<br>341 White St.<br>Daytons Beach, FL 32014<br>(904) 255-5444                     | Wisconsin  | American Red Cross<br>Blood Services<br>Badger Region<br>1202 Ann St.<br>Madison, WI 53713<br>(608) 255-0021  |
| Alabama,<br>Mississippi | American Red Cross<br>Blood Services<br>Alabama Region<br>2225 Third Ave., N.<br>Birmingham, AL 35203<br>(205) 322-5661                      | Minnesota  | American Red Cross<br>Blood Services<br>St. Paul Region<br>100 S. Robert St.<br>St. Paul, MN 55107<br>(612) 291-6789<br>(612) 291-6767 (night)            |
| Indiana                 | American Red Cross<br>Blood Services<br>Fort Wayne Region<br>1212 E. California Rd.<br>Fort Wayne, IN 46825<br>(219) 482-3781                | Northern Illinois<br>(Chicago)                                   | American Red Cross<br>Blood Services<br>Mid-America Region<br>43 E. Ohio St.<br>Chicago, IL 60611<br>(312) 440-2222                                       |
| Michigan                | American Red Cross<br>Blood Services<br>Southeastern Michigan Region<br>100 Mack Ave.<br>P.O. Box 351<br>Detroit, MI 48232<br>(313) 494-2715 | Arkansas,<br>Kansas, Kentucky,<br>Missouri,<br>Southern Illinois | American Red Cross<br>Blood Services<br>Missouri-Illinois Region<br>4050 Lindell Blvd.<br>St. Louis, MO 63108<br>(314) 658-2000<br>(314) 658-2136 (night) |
| or                      | American Red Cross<br>Blood Services<br>Wolverine Region<br>202 E. Boulevard Dr.<br>Flint, MI 48501<br>(313) 232-1176                        | Nebraska   | American Red Cross<br>Blood Services<br>Midwest Region<br>3838 Dewey Ave.<br>Omaha, NE 68105<br>(402) 341-2723  |
| or                      | American Red Cross<br>Blood Services<br>Great Lakes Region<br>1800 E. Grand River<br>Lansing, MI 48912<br>(517) 484-7461                     | Tennessee  | American Red Cross<br>Blood Services<br>Nashville Region<br>321 22nd Ave., N.<br>Nashville, TN 37203<br>(615) 327-1931, ext. 315                          |
| Ohio                    | American Red Cross<br>Blood Services<br>Northern Ohio Region<br>3950 Chester Ave.<br>Cleveland, OH 44114<br>(216) 781-1800                   | Louisiana,<br>Oklahoma,<br>Texas                                 | Gulf Coast Regional<br>Blood Center<br>1400 La Concha<br>Houston, TX 77054-1802<br>(713) 791-6250   |

TABLE 4. Varicella-zoster immune globulin regional distribution centers — *Continued*

| Service area  | Regional center and 24-hour telephone   | Service area                 | Regional center and 24-hour telephone  |
|---|---|------------------------------|--|
| or  | American Red Cross<br>Blood Services<br>Central Texas Region<br>McLennan County Chapter<br>4224 Cobbs Dr.<br>Waco, TX 76710<br>(817) 776-8754 | Idaho                        | American Red Cross<br>Blood Services<br>Snake River Region<br>5380 Franklin St.<br>Boise, ID 83705<br>(208) 342-4500                   |
| or  | American Red Cross<br>Blood Services<br>Red River Region<br>1809 Fifth St.<br>Wichita Falls, TX 76301<br>(817) 322-8686                       | Washington                   | Puget Sound Blood Center<br>Terry at Madison<br>Seattle, WA 98104<br>(206) 292-6525  |
| Colorado,<br>New Mexico                             | United Blood Services<br>1515 University Blvd., N.E.<br>P.O. Box 25445<br>Albuquerque, NM 87125<br>(505) 247-9831                             | Canada                       | Canadian Red Cross<br>Blood Transfusion Service<br>National Office<br>95 Wellesley St. E.<br>Toronto, Ontario M4Y1H6<br>(416) 923-6692 |
| Arizona   | American Red Cross<br>Blood Services<br>Southern Arizona Region<br>222 South Cherry Ave.<br>Tucson, AZ 85719<br>(602) 623-0541                | Puerto Rico                  | American Red Cross<br>Servicio de Sangre Capitulo<br>GPO Box 6046<br>San Juan, PR 00936<br>(809) 759-7979                              |
| Hawaii,<br>Southern<br>California                   | American Red Cross<br>Blood Services<br>L.A.-Orange Counties Region<br>1130 S. Vermont Ave.<br>Los Angeles, CA 90006<br>(213) 739-5200        | Central and<br>South America | South Florida Community<br>Blood Center<br>1675 N.W. Ninth Ave.<br>Miami, FL 33142<br>(305) 326-8888                                   |
| Nevada, Utah,<br>Wyoming,<br>Northern<br>California | American Red Cross<br>Blood Services<br>Central California Region<br>333 McKendrie St.<br>San Jose, CA 95110<br>(408) 292-1626                | All other countries          | American Red Cross<br>Blood Services<br>Northeast Region<br>60 Kendrick St.<br>Needham, MA 02194<br>(617) 449-0773                     |
| Alaska, Montana,<br>Oregon                          | American Red Cross<br>Blood Services<br>Pacific Northwest Region<br>4200 S.W. Corbett St.<br>Portland, OR 97201<br>(503) 243-5286             | or                           | American Red Cross<br>Blood Services<br>812 Huntington Avenue<br>Boston, MA 02115<br>(617) 731-2130                                    |

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Centers for Disease Control  
Atlanta, Georgia 30333

## INTERNATIONAL TRAVEL

### GENERAL RECOMMENDATIONS AND CONSULTATION

The Communicable Disease Section of the MDHES provides consultation regarding immunizations and other health information related to international travel. The U.S. Department of Health and Human Services (HHS) has published the book, Health Information for International Travel which includes:

- Vaccine Information
- Vaccine Certificate Requirements
- U.S. Public Health Service Recommendations
- Specific Recommendations for Vaccination and Prophylaxis
- Geographical Description of Potential Health Hazards
- Geographical Description of Potential Health Hazards
- Health Hints for Travelers
- Importation or Exportation of Human Remains
- Reentry or Importation of Pets
- Subject Index; and
- Index by Country

A copy of Health Information for International Travel can be obtained from:

The Superintendent of Documents  
U.S. Government Printing Office  
Washington, D.C. 20402  
Phone: (202) 783-3238

A weekly summary of Countries with Areas Infected with Quarantinable Diseases According to the World Health Organization, a supplement of the Health Information for International Travel, includes information on countries infected with yellow fever, and cholera and those countries considered a threat to the introduction of plague.

A copy of the consultation sheet that is used by the Communicable Disease Section is attached.

### WHO PROVIDES INTERNATIONAL TRAVEL IMMUNIZATIONS?

Yellow fever vaccinations are only available from clinics that are authorized to provide the vaccine.

For those who wish to receive yellow fever vaccine, arrangements should be made in advance with the Yellow Fever Vaccine Centers to determine vaccine availability, cost, and clinic information. For information on yellow fever immunization contact the following:

In Butte:

Butte-Silver Bow County Health Department  
58 West Quartz  
Butte, MT 59701  
John Pullman, M.D.  
(406) 723-4022



Yellow Fever Vaccine (continued)

In Kalispell:

Flathead City-County Health Dept.  
723 Fifth Avenue East  
Kalispell, MT 59901  
(406) 752-5300

In Billings:

Yellowstone City-County Health Dept.  
Deering Community Health Center  
123 South 27th Street  
Billings, MT 59101  
(406) 256-6821

Doctor's Walk In Clinic  
1005 - 24th Street West  
Billings, MT 59102  
(406) 652-2224

In Great Falls:

Malmstrom Air Force Base  
U.S.A.F. Hospital (SGHL)  
Great Falls, MT 59402  
(406) 731-9990, 3757

In Helena:

Lewis & Clark City-County  
Health Dept.  
P. O. Box 1723  
316 North Park  
Helena, MT 59601  
(406) 443-1010

Cascade City-County Health Dept.  
1130 17th Avenue South  
Great Falls, MT 59405  
(406) 761-1190

In Missoula:

Missoula City-County Health Dept.  
301 West Alder Street  
Missoula, MT 59802  
(406) 721-6700

In Bozeman:

Gallatin County Health Department  
Courthouse, Room 103  
Bozeman, MT 59715  
(406) 585-1445

Vaccines, other than yellow fever, and medication that may be necessary or recommended for International travel may be obtained at other public clinics or through a private physician (i.e., malaria prophylaxis or measles immunization).

The Montana Immunization Program does not provide the immunization record International Certificate of Vaccination. However, they are available through local health departments that perform international travel vaccination.





## Yellow Fever

See the section "Who Provides International Immunizations" for clinics in Montana that provide Yellow Fever vaccine.

Refer to the book Health Information for International Travel for yellow fever requirements and recommendations.

See the attached ACIP statement on yellow fever vaccine. Also, see the Adult Immunization Recommendations on Yellow Fever Vaccine.



### Yellow Fever Vaccine

These revised Immunization Practices Advisory Committee (ACIP) recommendations on yellow fever vaccine update the previous recommendations (MMWR 1978;27:268-70). Changes have been made to clarify (1) the risks of acquiring yellow fever associated with travel to endemic areas; (2) the precautions necessary for immunization of special groups (infants, pregnant women); (3) procedures for immunization of persons with histories of possible egg allergy; and (4) simultaneous administration of other vaccines.

#### INTRODUCTION

Yellow fever presently occurs only in Africa and South America. Two forms of yellow fever—urban and jungle—are epidemiologically distinguishable. Clinically and etiologically, they are identical (1,2).

Urban yellow fever is an epidemic viral disease of humans transmitted from infected to susceptible persons by a vector, the *Aedes aegypti* mosquito. In areas where *Ae. aegypti* has been eliminated or suppressed, urban yellow fever has disappeared; eradication of *Ae. aegypti* in a number of countries, notably Panama, Brazil, Ecuador, Peru, Bolivia, Paraguay, Uruguay, and Argentina, achieved in the early 1900s, led to the disappearance of urban yellow fever. The last *Ae. aegypti*-borne yellow fever epidemic occurred in Trinidad in 1954. However, periodic reinfestations of some countries have occurred in recent years, and other countries remain infested, including areas of Venezuela, Colombia, and Guiana, which border on the enzootic zone for jungle yellow fever. In West Africa, *Ae. aegypti*-transmitted epidemics continue to occur at frequent intervals and involve human populations in both towns and rural villages (3).

Jungle yellow fever is an enzootic viral disease transmitted among nonhuman primate hosts by a variety of mosquito vectors. It is currently observed only in forest-savannah zones of tropical Africa and in forested areas of South America, but occasionally extends into parts of Central America and the island of Trinidad. In South America, approximately 200-400 cases are recognized annually, mainly among persons with occupational exposures in forested areas; the disease is, however, believed to be greatly underreported. In Africa, epidemics involving forest mosquito vectors affect tens of thousands of persons at intervals of a few years, but few cases are officially reported. The disease may sometimes not be detected in an area for some years and then reappear. Delineation of affected areas depends on surveillance of animal reservoirs and vectors, accurate diagnosis, and prompt reporting of all cases. The jungle yellow fever cycle may be active but unrecognized in forested areas of countries within the yellow fever endemic zone (Figure 2).

Urban yellow fever can be prevented by eradicating *Ae. aegypti* mosquitoes or by suppressing their numbers to the point that they no longer perpetuate infection. At the present time, jungle yellow fever can most effectively be prevented in humans by immunization.

#### YELLOW FEVER VACCINE

Yellow fever vaccine\* is a live, attenuated virus preparation made from the 17D yellow fever virus strain (4). The 17D vaccine has proven to be extremely safe and effective (5). The

\*Official name: Yellow Fever Vaccine.

FIGURE 2. Yellow fever endemic zones in Americas and Africa and number of yellow fever cases reported to World Health Organization, 1965-1980



17D strain is grown in chick embryo inoculated with a seed virus of a fixed-passage level. The vaccine is freeze-dried supernate of centrifuged embryo homogenate, packaged in one-dose and five-dose vials for domestic use.

Vaccine should be stored at temperatures between 5 C (41 F) and -30 C (-22 F)—preferably frozen, below 0 C (32 F)—until it is reconstituted by the addition of diluent sterile, physiologic saline supplied by the manufacturer. Multiple dose vials of reconstituted vaccine should be held at 5 C-10 C (41 F-50 F); unused vaccine should be discarded within 1 hour after reconstitution.

#### VACCINE USAGE

##### A. Persons living or traveling in endemic areas:

1. Persons 6 months of age or older traveling or living in areas where yellow fever infection exists—currently parts of Africa and South America—should be vaccinated. (These are listed in the "Bi-Weekly Summary of Countries with Areas Infected with Quarantinable Diseases" available in state and local health departments. Information on known or probable infected areas is also available from the World Health Organization [WHO] and Pan American Health Organization offices or the Division of Vector-Borne Viral Diseases, Center for Infectious Diseases, CDC, Fort Collins, Colorado.)

Vaccination is also recommended for travel outside the urban areas of countries in the yellow fever endemic zone (Figure 1). It should be emphasized that the actual areas of yellow fever virus activity far exceed the infected zones officially reported and that, in recent years, fatal cases of yellow fever have occurred in unvaccinated tourists (6).

2. Infants under 6 months of age and pregnant women should be considered for vaccination if traveling to high-risk areas when travel cannot be postponed and a high level of prevention against mosquito exposures is not feasible.
3. Laboratory personnel who might be exposed to virulent yellow fever virus should also be vaccinated.

##### B. Vaccination for international travel: For purposes of international travel, yellow fever vaccines produced by different manufacturers worldwide must be approved by WHO and administered at an approved Yellow Fever Vaccination Center. State and territorial health departments have the authority to designate nonfederal vaccination centers; these can be identified by contacting state or local health departments. Vaccinees should have an International Certificate of Vaccination filled in, signed, and validated with the center's stamp where the vaccine is given.

Vaccination for international travel may be required under circumstances other than those specified herein. Some countries in Africa require evidence of vaccination from all entering travelers. Some countries may waive the requirements for travelers coming from noninfected areas and staying less than 2 weeks. These requirements may change, so all travelers should seek current information from health departments. Travel agencies, international airlines, and/or shipping lines should also have up-to-date information.

Some countries require an individual, even if only in transit, to have a valid International Certificate of Vaccination if he or she has been in countries either known or thought to harbor yellow fever virus. Such requirements may be strictly enforced, particularly for persons traveling from Africa or South America to Asia.

- C. Primary immunization: For persons of all ages, a single subcutaneous injection of 0.5 ml of reconstituted vaccine is used.
- D. Booster doses: Yellow fever immunity following vaccination with 17D strain virus persists for more than 10 years (7-9); the International Health Regulations do not require vaccination more often than every 10 years.

#### REACTIONS

Reactions to 17D yellow fever vaccine are generally mild. Two percent to 5% of vaccinees have mild headaches, myalgia, low-grade fevers, or other minor symptoms 5-10 days after vaccination. Fewer than 0.2% curtail regular activities. Immediate hypersensitivity reactions, characterized by rash, urticaria, and/or asthma, are extremely uncommon (incidence less than 1/1,000,000) and occur principally in persons with histories of egg allergy. Although more than 34 million doses of vaccines have been distributed, only two cases of encephalitis temporally associated with vaccinations have been reported in the United States; in one fatal case, 17D virus was isolated from the brain.

#### PRECAUTIONS AND CONTRAINDICATIONS

- A. Age: Infants under 6 months of age are theoretically more susceptible to serious adverse reactions (encephalitis) than older children.
- B. Pregnancy: Although specific information is not available concerning adverse effects of yellow fever vaccine on the developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women and to postpone travel to areas where yellow fever is present until after delivery. If international travel requirements constitute the only reason to vaccinate a pregnant woman, rather than an increased risk of infection, efforts should be made to obtain a waiver letter from the traveler's physician (see below). Pregnant women who must travel to areas where the risk of yellow fever is high should be vaccinated. It is believed that under these circumstances, the small theoretical risk for mother and fetus from

vaccination is far outweighed by the risk of yellow fever infection.

C. **Altered immune states:** Infection with yellow fever vaccine virus poses a theoretical risk to patients with leukemia, lymphoma, or generalized malignancy or to those whose immunologic responses are suppressed by corticosteroids, alkylating drugs, antimetabolites, or radiation. Short-term (less than 2 weeks) corticosteroid therapy or intra-articular, bursal, or tendon injections with corticosteroids should not be immunosuppressive and constitute no increased hazard to recipients of yellow fever vaccine.

D. **Hypersensitivity:** Live yellow fever vaccine is produced in chick embryos and should not be given to persons clearly hypersensitive to eggs; generally, persons who are able to eat eggs or egg products may receive the vaccine.

If international travel regulations are the only reason to vaccinate a patient hypersensitive to eggs, efforts should be made to obtain a waiver. A physician's letter clearly stating the contraindication to vaccination has been acceptable to some governments. (Ideally, it should be written on letterhead stationery and bear the stamp used by health departments and official immunization centers to validate the International Certificates of Vaccination.) Under these conditions, it is also useful for the traveler to obtain specific and authoritative advice from the country or countries he or she plans to visit. Their embassies or consulates may be contacted. Subsequent waiver of requirements should be documented by appropriate letters.

If vaccination of an individual with a questionable history of egg hypersensitivity is considered essential because of a high risk of exposure, an intradermal test dose may be administered under close medical supervision. Specific directions for skin testing are found in the package insert.

#### SIMULTANEOUS ADMINISTRATION OF OTHER VACCINES

Determination of whether to administer yellow fever vaccine and other immunobiologics simultaneously should be made on the basis of convenience to the traveler in completing the desired immunizations before travel and on information regarding possible interference. The following will help guide these decisions.

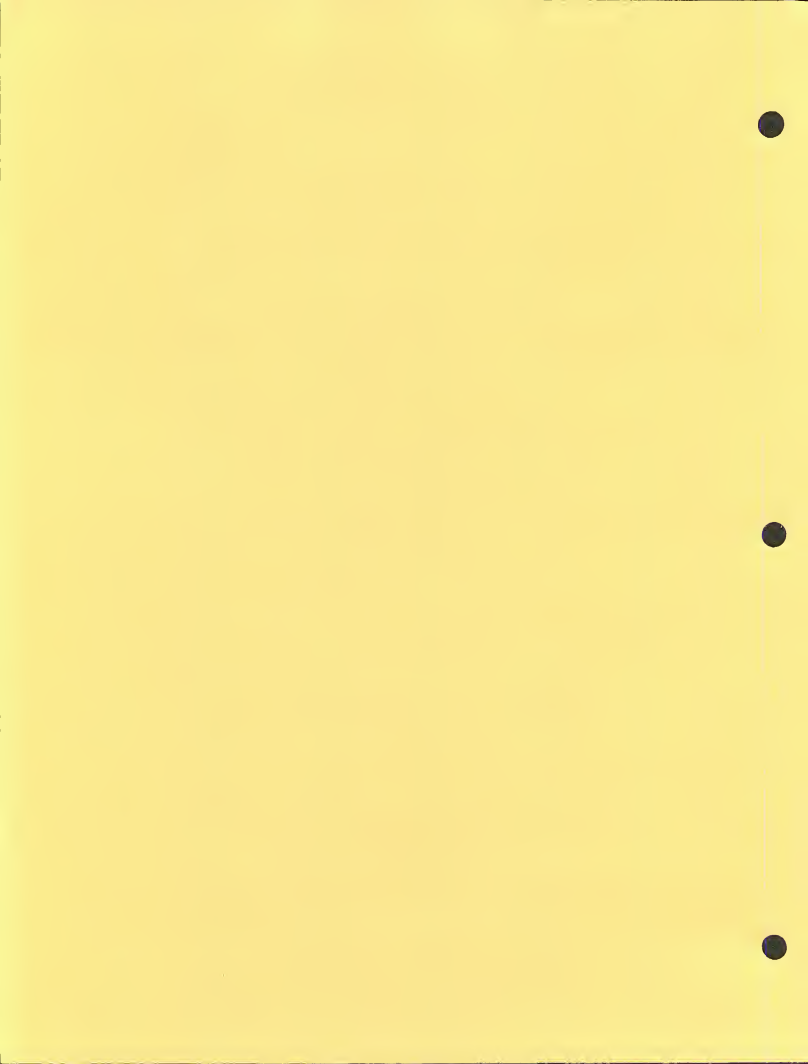
Studies have shown that the serologic response to yellow fever vaccine is not inhibited by administration of certain other vaccines concurrently or at various intervals of a few days to 1 month. Measles, smallpox, and yellow fever vaccines have been administered in combination with full efficacy of each of the components; Bacillus Calmette Guérin (BCG) and yellow fever vaccines have been administered simultaneously without interference. Additionally, severity of reactions to vaccination was not amplified by concurrent administration of yellow fever and other live virus vaccines (10). If live virus vaccines are not given concurrently, 4 weeks should be allowed to elapse between sequential vaccinations.

Other studies have indicated that persons given yellow fever and cholera vaccines simultaneously or 1-3 weeks apart showed reduced antibody responses to both vaccines (11, 12). When feasible, cholera and yellow fever vaccines should be administered at a minimal interval of 3 weeks, unless time constraints preclude this. If the vaccines cannot be administered at least 3 weeks apart, they should be given simultaneously. There are no data on possible interference between yellow fever and typhoid, paratyphoid, typhus, hepatitis B, plague, rabies, or Japanese encephalitis vaccines.

A recently completed prospective study of persons given yellow fever vaccine and 5 cc of commercially available immune globulin revealed no alteration of the immunologic response to yellow fever vaccine when compared to controls (13).

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### Cholera

Refer to the book Health Information for International Travel and the weekly summary for information on countries that have recently reported cholera.

The MDHES does not recommend the use of cholera vaccine for either routine use or travel to or from cholera infected areas. See the attached ACIP statement on cholera vaccine. Also see the Adult Immunization Recommendations on cholera vaccine and the Control of Communicable Diseases in Man.





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Recommendations of the Immunization  
Practices Advisory Committee

**Cholera Vaccine**

**INTRODUCTION**

Historically, endemic and epidemic cholera commonly has occurred in parts of southern and southeastern Asia. Since 1961, cholera caused by the El Tor biotype has been epidemic throughout much of Asia, the Middle East, and Africa and in certain parts of Europe. Infection is acquired primarily by consuming contaminated water or food; person-to-person transmission is rare. Travelers who follow the usual tourist itinerary and who use standard accommodations in countries affected by cholera are at virtually no risk of infection.

**CHOLERA VACCINE**

Cholera vaccines\*, whether prepared from Classic or El Tor strains, are of limited usefulness. In field trials conducted in areas with endemic cholera, vaccines have been only about 50% effective in reducing the incidence of clinical illness for 3-6 months. They do not prevent transmission of infection. Therefore, the Public Health Service no longer requires cholera vaccination for travelers coming to the United States from cholera-infected areas, and the World Health Organization (WHO) no longer recommends cholera vaccination for travel to or from cholera-infected areas. Surveillance and treatment are sufficient to prevent spread of the disease if it were introduced into the United States.

Vaccine available in the United States is prepared from a combination of phenol-inactivated suspensions of classic Inaba and Ogawa strains of *Vibrio cholerae* grown on agar or in broth.

**VACCINE USAGE**

**General Recommendations**

Vaccine should not be used to manage contacts of persons with imported cases or to control the spread of infection. Repeated vaccination is required or advised sometimes for laboratory workers and airline and ship crews. However, such groups are unlikely to acquire or transmit cholera. Because information on the long-term safety of repeated vaccination is limited, such practices should be discontinued for airline and ship crews except when resolutely demanded by some countries for international travel.

Vaccine is not recommended for infants <6 months of age and is not required for travel by most countries.

**Vaccination for International Travel**

The risk of cholera to U.S. travelers is so low that the vaccine is not likely to benefit most U.S. travelers. Persons using standard tourist accommodations in countries affected by cholera are at virtually no risk of infection. The traveler's best protection against cholera, as well as against many other enteric diseases, is to avoid food and water that might be contaminated.

However, many countries affected or threatened by cholera require evidence of cholera vaccination for entry. One dose of vaccine will usually satisfy entry requirements for persons who anticipate travel to such countries and who will be vaccinated in the United States.

With the threat or occurrence of epidemic cholera, health authorities of some countries may require evidence of a complete primary series of two doses or a booster dose within 6 months before arrival. The complete primary series is otherwise suggested only for special high-risk groups that work and live in highly endemic areas under less than sanitary conditions (Table 1).

Vaccination requirements published by WHO are regularly updated and summarized for travelers by the Public Health Service and distributed to state and local health departments, airlines, travel agents, many physicians, and others. Physicians and travelers should seek information on requirements from these sources.

\*Official name: Cholera Vaccine.

Physicians administering vaccine to travelers should emphasize that an International Certificate of Vaccination against cholera must be validated for it to be acceptable to quarantine authorities. Validation can be obtained at most city, county, and state health departments as well as many private clinics and physicians' offices. Failure to secure validation may cause travelers to be revaccinated or quarantined. A properly documented certificate is valid for 6 months, beginning 6 days after vaccination or beginning on the date of revaccination if this revaccination is within 6 months of a previous injection.

Data have indicated that persons given yellow fever and cholera vaccines simultaneously or 1-3 weeks apart had initially lower-titered antibody responses to both vaccines. However, seroconversion rates were unaffected, and the clinical importance of these data are unknown. In view of these data, yellow fever and cholera vaccines ideally should be given at least 3 weeks apart. If that is not possible, and both vaccines must be given, then they can be given simultaneously or at any time within the 3-week interval, although a delay in expected yellow fever protection may occur.

#### Primary Immunization

Complete primary immunization consists of two doses of vaccine given at least 1 week apart. The intradermal route is satisfactory for persons  $\geq 5$  years of age (Table 1).

#### Booster Doses

Booster doses may be given every 6 months if necessary for travel or for residence in highly endemic, unsanitary areas. In areas where cholera occurs in a 2-3 month season, protection is best if the booster dose is given at the beginning of the season. The primary series does not need to be repeated for booster doses to be effective.

### PRECAUTIONS AND CONTRAINDICATIONS

#### Reactions

Vaccination often results in 1-2 days of pain, erythema, and induration at the site of injection. The local reaction may be accompanied by fever, malaise, and headache.

Serious reactions following cholera vaccination are extremely rare. If a person has had a serious reaction to the vaccine, revaccination is not advised. Most governments will permit an unvaccinated traveler to proceed if he/she carries a physician's statement of medical contraindication. However, some countries may quarantine such unvaccinated persons or place them under surveillance if they come from areas with cholera.

#### Pregnancy

No specific information exists on the safety of cholera vaccine during pregnancy. Its use should be individualized to reflect actual need.

TABLE 1. Recommended doses, by volume, for immunization against cholera

| Dose no. | Route and age |                               |             |          |
|----------|---------------|-------------------------------|-------------|----------|
|          | Intradermal*  | Subcutaneous or intramuscular |             |          |
|          |               | <5 yrs                        | 6 mos-4 yrs | 5-10 yrs |
| 1 and 2  | 0.2 mL        | 0.2 mL                        | 0.3 mL      | 0.5 mL   |
| Boosters | 0.2 mL        | 0.2 mL                        | 0.3 mL      | 0.5 mL   |

\*Higher levels of protection (antibody) may be achieved in children <5 years old by the subcutaneous or intramuscular routes.

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## Typhoid

Refer to the book Health Information for International Travel.

The MDHES does not recommend the use of typhoid vaccine for persons in the United States nor for use in routine international travel.

See the attached ACIP statement on typhoid vaccine. Also, see the Adult Immunization Recommendations on typhoid vaccine and the Control of Communicable Diseases in Man.



Recommendation of the Public Health Service  
Advisory Committee on Immunization Practices

Typhoid Vaccine

**INTRODUCTION**

The incidence of typhoid fever has declined steadily in the United States in the last half century, and in recent years fewer than 400 cases have been reported annually. The continuing downward trend is due largely to better sanitation and other control measures; vaccine is not deemed to have played a significant role. An increasing proportion of cases reported in the United States (about 50% in 1976) were acquired by travelers in other countries.

**TYPHOID AND PARATYPHOID A AND B VACCINES**

Although typhoid vaccines\* have been used for many decades, only recently has definitive evidence of their effectiveness been observed in well-controlled field investigations. Several different preparations of typhoid vaccine have been shown to protect 70-90% of recipients, depending in part of the degree of their subsequent exposure.

The effectiveness of paratyphoid A vaccine has never been established, and field trials have shown that usually small amounts of paratyphoid B antigens contained in "TAB" vaccines (vaccines combining typhoid and paratyphoid A and B antigens) are not effective. Knowing this and recognizing that combining paratyphoid A and B antigens with typhoid vaccine increases the risk of vaccine reaction, one should use typhoid vaccine alone.

**VACCINE USAGE**

Routine typhoid vaccination is no longer recommended for persons in the United States. Selective immunization is, however, indicated for:

1. Persons with intimate exposure to a documented typhoid carrier, such as would occur with continued household contact.

2. Travelers to areas where there is a recognized risk of exposure to typhoid because of poor food and water sanitation. It should be emphasized, however, that even after typhoid vaccination there should be careful selection of foods and water in these areas.

There is no evidence that typhoid vaccine is of value in the United States in controlling common-source outbreaks. Furthermore, there is no reason to use typhoid vaccine for persons in areas of natural disaster such as floods or for persons attending rural summer camps.

**Primary Immunization**

On the basis of the field trials referred to above, the following dosages of typhoid vaccine available in the United States are recommended:

Adults and children 10 years and older: 0.5 ml subcutaneously on 2 occasions, separated by 4 or more weeks.

Children less than 10 years old\*: 0.25 ml subcutaneously on 2 occasions, separated by 4 or more weeks.

In instances where there is not sufficient time for 2 doses at the interval specified, it has been common practice to give 3 doses of the same volumes listed above at weekly intervals, although it is recognized that this schedule may be less effective. When vaccine must be administered for travel overseas under constraint of time, a second dose may be administered en route at the more desirable interval.

**Booster Doses**

Under conditions of continued or repeated exposure, a booster dose should be given at least every 3 years. Even when more than a 3-year interval has elapsed since the prior immunization, a single booster injection is sufficient.

The following alternate routes and dosages of booster immunization can be expected to produce comparable antibody responses. Generally less reaction follows vaccination by the intradermal route, except when acetone-killed and dried vaccine is used. (The latter vaccine should not be given intradermally.)

Adults and children 10 years and older: 0.5 ml subcutaneously or 0.1 ml intradermally.

Children 6 months to 10 years: 0.25 ml subcutaneously or 0.1 ml intradermally.

## PRECAUTIONS AND CONTRAINDICATIONS

Typhoid vaccination often results in 1-2 days of discomfort at the site of injection. The local reaction may be accompanied by fever, malaise, and headache.

\*Since febrile reactions to typhoid vaccine are common in children, an antipyretic may be indicated.

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Published in *MMWR* 15:247, 1966; revised 18(43 Suppl):26, 1969; revised 21(25 Suppl):38-39, 1972

## Plague

Refer to the book Health Information for International Travel and the weekly summary for information on countries that are considered a threat in the introduction of plague.

The MDHES does not recommend the use of plague vaccine for either routine use or travel to countries listed on the summary sheet that are "considered a threat to the introduction of plague."

See the attached ACIP statement on plague vaccine. Also, see the Adult Immunization Recommendations on plague vaccine and the Control of Communicable Diseases in Man.





## Plague Vaccine

These revised ACIP recommendations on plague vaccine represent an update of the previous recommendations (MMWR 1978;27:255-8) to include current information and practices.

### INTRODUCTION

Plague is a natural infection of rodents and their ectoparasites and occurs in many parts of the world, including the western United States. In this country, a few human cases develop each year following exposure to infected wild rodents or their fleas and, less commonly, to other infected wild animals (bobcats, coyotes, rabbits) and domestic animals (cats, dogs). Epidemic plague may result when domestic rat populations and their fleas become infected. Recently, the areas of the most intensive epidemic and epizootic infection have been some countries in Africa, Asia, and South America.

Because human plague is rare in most parts of the world, there is no need to vaccinate persons other than those at particularly high risk of exposure. Routine vaccination is not necessary for persons living in areas with enzootic plague such as the western United States. It is not indicated for most travelers to countries reporting cases,\* particularly if their travel is limited to urban areas with modern hotel accommodations.

Many plague patients in the western United States are infected as a direct result of wild-rodent plague in the immediate vicinity of their homes. Recommended risk-reduction measures include eliminating wild-rodent harborage and food sources near homes, ridding pet dogs and cats of fleas at least weekly, and avoiding direct contact with sick or dead rodents.

In most countries of Africa, Asia, and South America where plague is reported, the risk of exposure exists primarily in rural mountainous or upland areas. Following natural disasters and at times when regular sanitary practices are interrupted, plague can extend from its usual areas of endemicity into urban centers. Rarely, pneumonic plague has been reported in conjunction with outbreaks of bubonic plague, and tourist travel to areas with reported cases of plague should be avoided.

Routine bacteriologic precautions, including the use of a biological safety cabinet to isolate procedures that may produce aerosols, are sufficient to prevent accidental infection with plague among clinical laboratory workers. Few laboratory-associated cases have ever been reported, and these almost exclusively occurred at plague research laboratories or involved unusual exposures. Vaccination of clinical laboratory workers is not indicated.

Ecologists and other field workers who might come in contact with wild animals and their ectoparasites in areas where plague has been known to occur should be made aware of the potential risks of plague and told how to minimize direct contact with potentially infective animals and their tissues or parasites. These precautionary measures are generally sufficient to prevent infection.

### PLAGUE VACCINE

Plague vaccines<sup>†</sup> have been used since the late 19th century, but their effectiveness has never been measured precisely. Field experience indicates that vaccination with plague vaccine reduces the incidence and severity of disease resulting from the bite of infected fleas. The degree of protection afforded against primary pneumonic infection is not known. Persons exposed to plague patients who have pneumonia or to *Yersinia pestis* aerosols in the laboratory should be given a 7- to 10-day course of antimicrobial therapy regardless of vaccination history. Recommended antimicrobials include tetracyclines, chloramphenicol, or streptomycin.

The plague vaccine licensed for use in the United States is prepared from *Y. pestis* organisms grown in artificial media, inactivated with formaldehyde, and preserved in 0.5% phenol. The vaccine contains trace amounts of beef-heart extract, yeast extract, agar, and peptones and peptides of soya and casein.

Serum antibody to Fraction I capsular antigen, as measured by the passive hemagglutination (PHA) test, is correlated with resistance to *Y. pestis* infection in experimental animals. A comparable correlation between PHA titer and immunity probably occurs in humans.

Following the primary series of 3 injections, about 7% of individuals do not produce PHA

\*For a current listing, consult the most recent issue of the World Health Organization's *Weekly Epidemiological Record*; current information is also available from the Quarantine Division, Center for Prevention Services, Centers for Disease Control, Atlanta, Georgia 30333.

<sup>†</sup>Official name: Plague Vaccine

<sup>‡</sup>The designation *Yersinia pestis* is used advisedly since there is reportedly a recommendation by the International Committee on Systematic Bacteriology to reclassify this organism as *Yersinia pseudotuberculosis* ssp. *pestis* (WHO, *Weekly Epidemiological Record* 1981;56:399).

antibody, and a few fail to develop a titer of 128, the level correlated with immunity in experimental animals. PHA titers should be determined for individuals who have an unusually high risk of infection or who have a history of serious reactions to the vaccine in order to govern the frequency of booster doses. Such testing can be arranged through state health departments. Since plague vaccination may only ameliorate illness, whenever a vaccinated person has a definite exposure, prophylactic antibiotics may be indicated whether or not an antibody response has been demonstrated.

#### Vaccine Recipients

Vaccination is recommended for:

1) All laboratory and field personnel who are working with *Y. pestis* organisms resistant to antimicrobics, 2) Persons engaged in aerosol experiments with *Y. pestis* and 3) Persons engaged in field operations in areas with enzootic plague where preventing exposure is not possible (such as some disaster areas).

Selective plague vaccination should be considered for:

1) Laboratory personnel regularly working with *Y. pestis* or plague-infected rodents, 2) Workers (for example, Peace Corps volunteers and agricultural advisors) who reside in rural areas with enzootic or epidemic plague where avoidance of rodents and fleas is impossible, and 3) Persons whose vocation brings them into regular contact with wild rodents or rabbits in areas with enzootic plague.

#### Primary Vaccination

All injections should be given intramuscularly.

**Adults and children  $\geq 11$  years old:** The primary series consists of 3 doses of vaccine. The first dose, 1.0 ml, is followed by the second dose, 0.2 ml, 4 weeks later. The third dose, 0.2 ml, is administered 6 months after the first dose. If an accelerated schedule is essential, 3 doses of 0.5 ml each, administered at least 1 week apart, may be given. The efficacy of this schedule has not been determined.

**Children  $\geq 10$  years old:** The primary series is also 3 doses of vaccine, but the doses are smaller (Table 1). The intervals between injections are the same as for adults.

#### Booster Doses

When needed because of continuing exposure, 3 booster doses should be given at approximately 6-month intervals. Thereafter, antibody levels decline slowly and booster doses at 1- to 2-year intervals, depending on the degree of continuing exposure, should provide good protection.

The recommended booster dosages for children and adults are the same as the second and third doses in the primary series. However, if serious side effects to the vaccine occur, their severity may be reduced by using half the usual dose. The primary series need never be repeated for booster doses to be effective (Table 2).

#### SIDE EFFECTS OF VACCINE

Primary vaccination may result in general malaise, headache, fever, mild lymphadenopathy, and arthralgia and induration at the injection site in about 10% of recipients. These reactions occur more commonly with repeated injections. Sterile abscesses occur rarely. Rare cases of sensitivity reactions manifested by urticarial and asthmatic phenomena have been reported.

#### PRECAUTIONS AND CONTRAINDICATIONS

Plague vaccine should not be administered to anyone with a known hypersensitivity to any of the constituents, such as beef protein, soya, casein, and phenol. Patients who have had severe local or systemic reactions to plague vaccine should not be revaccinated.

The safety or efficacy of vaccination with plague vaccine during pregnancy has not been determined, and therefore it should not be used unless there is a substantial risk of infection.

TABLE 2. Plague vaccine doses (in milliliters), by age group (in years), for primary and booster vaccinations\*

| Dose number | <1        | 1-4       | 5-10      | >11     |
|-------------|-----------|-----------|-----------|---------|
| I           | 0.2       | 0.4       | 0.6       | 1.0     |
| 2 & 3       | 0.04      | 0.08      | 0.12      | 0.2     |
| Boosters†   | 0.02-0.04 | 0.04-0.08 | 0.06-0.12 | 0.1-0.2 |

\*Important details are in the text.

†Smaller dose volume may be used if severe side effects are expected.

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Smallpox

The MDHES does not recommend the use of smallpox vaccine except as indicated in the attached ACIP statement on smallpox vaccine. Also, refer to the Control of Communicable Diseases in Man.



## Smallpox Vaccine

*These revised ACIP recommendations on smallpox vaccine update the previous recommendations (MMWR 1980;29:417-20) to include current information on the changes in the international Health Regulations and the ending of distribution of smallpox vaccine to civilians. The basic recommendation is unchanged—smallpox vaccine is only indicated for civilians who are laboratory workers occupationally exposed to smallpox or other closely related orthopox viruses.*

### SMALLPOX VACCINE

Smallpox vaccine (vaccinia virus) is a highly effective immunizing agent against smallpox. The judicious use of smallpox vaccine has eradicated smallpox. At the World Health Assembly in May 1980, the World Health Organization (WHO) declared the world free of smallpox (1-4). Smallpox vaccination of civilians is now indicated *only* for laboratory workers directly involved with smallpox (variola virus) or closely related orthopox viruses (e.g., monkeypox, vaccinia, and others).

### SURVEILLANCE OF SUSPECTED CASES OF SMALLPOX

There is no evidence of smallpox transmission anywhere in the world. WHO has coordinated the investigation of 173 rumors of smallpox between 1979 and 1984 (5-7). All have been diseases other than smallpox, most commonly chickenpox or other rash illnesses. Even so, a suspected case of smallpox is a public health emergency and must be promptly investigated. Assistance in the clinical evaluation, collection of laboratory specimens, and preliminary laboratory diagnosis is available from state health departments and CDC (telephone: (404) 329-3145 during the day and (404) 329-2888 outside usual working hours).

### MISUSE OF SMALLPOX VACCINE

There is no evidence that smallpox vaccination has any value in the treatment or prevention of recurrent herpes simplex infection, warts, or any disease other than those caused by orthopox viruses (8). Misuse of smallpox vaccine to treat herpes infections has been associated with severe complications (9-11). Smallpox vaccine should never be used therapeutically.

### SMALLPOX VACCINATION NOT REQUIRED FOR INTERNATIONAL TRAVEL

Smallpox vaccination is no longer required for international travel. In January 1982, the International Health Regulations were changed deleting smallpox from the Regulations (12). The International Certificates of Vaccination no longer include a smallpox vaccination certificate.

### SMALLPOX VACCINE NO LONGER AVAILABLE FOR CIVILIANS

In May 1983, the only active, licensed producer of smallpox vaccine in the United States discontinued distribution of smallpox vaccine to civilians (13). As a result, smallpox vaccine is no longer available to civilians.

### SMALLPOX VACCINE AVAILABLE TO PROTECT AT-RISK LABORATORY WORKERS

CDC provides smallpox vaccine to protect laboratory workers occupationally exposed to smallpox virus and other closely related orthopox viruses (14). Vaccine will be provided *only* for the protection of personnel of such laboratories. The vaccine should be administered to eligible employees under the supervision of a physician selected by the laboratory. Vaccine will be shipped to physicians responsible for vaccinating at-risk workers. Requests for vaccine should be sent to:

Drug Immunobiologic and Vaccine Service  
Center for Infectious Diseases  
Building 1, Room 1259  
Centers for Disease Control  
Atlanta, Georgia 30333  
(404) 329-3356

### SMALLPOX VACCINATION OF MILITARY PERSONNEL

U.S. military personnel are routinely vaccinated against smallpox.

### CONSULTATION FOR COMPLICATIONS OF SMALLPOX VACCINATION

CDC can assist physicians in the diagnosis and management of patients with suspected complications of smallpox vaccination. Vaccinia immune globulin (VIG) is available when indicated. Physicians should call (404) 329-3145 during the day and (404) 329-2888 evenings and weekends.

The majority of persons with such complications are likely to be recently vaccinated military personnel or their contacts infected through person-to-person spread of vaccinia virus (15-17). Such person-to-person spread can be extremely serious if the person infected has eczema or is immunocompromised.

Health-care workers are requested to report complications of smallpox vaccination to CDC through state and local health departments.

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Recommendations of the Immunization  
Practices Advisory Committee (ACIP)

**Use of BCG Vaccines in the Control of Tuberculosis:  
A Joint Statement by the ACIP  
and the Advisory Committee for Elimination of Tuberculosis**

Since 1979, when the last Immunization Practices Advisory Committee (ACIP) statement on vaccination with *Bacillus of Calmette and Guérin* (BCG\*) was published, additional data have been published on the epidemiology of tuberculosis (TB) in the United States and on the efficacy of childhood BCG vaccines. As a result, ACIP and the Advisory Committee for Elimination of Tuberculosis have issued the following educational update on BCG vaccines.<sup>1</sup>

Immunization with BCG vaccine lowers the risk of serious complications of primary TB in children (1-4). However, BCG vaccination should be considered only for children with negative tuberculin skin tests who fall into the following categories: 1) those who cannot be placed on isoniazid preventive therapy but who have continuous exposure to persons with active disease; 2) those with continuous exposure to patients with organisms resistant to isoniazid and rifampin; or 3) those belonging to groups with exceptionally high annual rates of new infection (i.e., >1% per year).

BCG vaccination is no longer recommended for health-care workers or other adults at high risk for acquiring TB infection. In addition, BCG should not be given to persons who are immunocompromised, including those with human immunodeficiency virus (HIV) infection.

## INTRODUCTION

### Transmission and Pathogenesis of TB

TB is a bacterial disease caused by organisms of the *Mycobacterium tuberculosis* complex (i.e., *M. tuberculosis*, *M. bovis*, *M. africanum*). It is transmitted primarily by airborne droplets; infection occurs when susceptible persons inhale infectious droplets produced by the exhalations of persons with respiratory tract TB. The risk for infection is directly related to duration and intensity of exposure to air contaminated with these droplets. TB infection usually begins in the lungs and spreads to the hilar lymph nodes, then to the blood stream. Thus, disease can occur in any organ of the body. Most infected persons react to the purified protein derivative (PPD) tuberculin skin test, and 5%-40% will develop clinically apparent TB. Infection is more likely to progress to clinical disease in the presence of certain risk factors, including younger and older ages, male sex, infection within the past 2 years, leanness, and suppression of cell-mediated immunity.

TB can be presumptively diagnosed if acid-fast bacilli are found in sputum, body fluids, or tissue or if at least two of three other conditions are met: 1) symptoms are compatible with TB; 2) chest radiograph is abnormal or abnormalities are found on physical examination; or 3) reaction to the tuberculin skin test is positive. Definitive diagnosis requires isolation and identification of organisms of the *M. tuberculosis* complex from a clinical specimen. Diagnosis of extrapulmonary TB is more difficult because it requires tissue biopsies or body fluids (e.g., spinal fluid) that usually contain only a few organisms.

### Epidemiology of TB in the United States

TB in the United States has declined approximately 6% per year since nationwide reporting began in 1953. However, in 1986, the morbidity rate for TB increased slightly to 9.4/100,000, a rate 82% lower than that for 1953 but 1.1% higher than the 1985 rate. A total of 22,768 cases were reported (5), and approximately 80% were pulmonary disease.

\*Official name: BCG Vaccine.

<sup>1</sup>Replaces previous recommendation on BCG vaccines (MMWR 1979;28:241-4).

Untreated TB is fatal in up to 50% of cases. However, chemotherapy has helped reduce the case-mortality rate 94% since 1953. In 1984, the most recent year for which final mortality data are available, 1729 deaths were attributed to TB, representing a mortality rate of 0.7/100,000 population.

Prevalence of TB infection and disease varies for different segments of the population. Disease rates are twice as high in males as in females and increase sharply with age in both sexes and all races. Groups at high risk for TB include most racial/ethnic minorities, immigrants from countries with a high prevalence of TB, the homeless population, close contacts of persons with pulmonary TB, and persons with HIV infection. In 1986, 62% of all TB cases occurred in racial/ethnic minorities, and over 20% of all cases were in foreign-born persons (5). Although the prevalence of active TB in the homeless population is difficult to assess, surveillance of selected clinics and shelters showed infection rates between 1.6% and 6.8% (6). Based on 1985 data from U.S. health departments, 29% of close contacts of TB patients were infected at the time the patients were diagnosed (7). In addition, the estimated risk for active TB in persons with symptomatic HIV infection is 100–200 times greater than that of persons in the general population (8). Persons with asymptomatic HIV infection and *M. tuberculosis* infection may have an equally high risk for developing clinical disease.

In 1985, the 1261 cases of TB in children <15 years of age accounted for 5.7% of cases in all age groups. Eighty percent of these were among racial/ethnic minorities (9). One fourth (315) of all childhood cases were extrapulmonary; of these, 41 cases were meningeal, and 17 were milary. Childhood cases of TB meningitis and milary TB remained stable between 1981 and 1985, averaging 55 cases annually.

In the past, TB was regarded as an occupational hazard for health-care workers, who had higher rates of infection and disease than persons of the same age groups in the general population. Although these rates have decreased over time, persons who work with high-risk patients or in high-prevalence communities still may be at risk for new infection, defined as conversion from a negative to a positive tuberculin skin test (10–18). However, in recent studies, which found increased conversion rates among health-care personnel, rates were highest in health-care workers who did not have patient contact (10,11), suggesting that conversion resulted from community-acquired infection with *M. tuberculosis* or exposure to nontuberculous mycobacteria rather than from occupational exposure.

#### Control of TB

There are four general strategies for controlling TB:

1. The most important and universally applied strategy is the early identification and treatment of persons with infectious TB. This strategy not only cures the affected person but also renders the patient noncontagious within a few weeks. Thus, case-finding and treatment programs have both clinical and public health benefits (19).
2. Identifying and treating persons with noncontagious TB (such as extrapulmonary disease, primary pulmonary disease in children, bacteriologically unconfirmed pulmonary disease, and tuberculous infection) can prevent infectious cases (20). Therapy to prevent progression of infection to clinical disease is particularly useful in countries, such as the United States, where the risk of new infection is low.
3. Use of ventilation and ultraviolet lights will decontaminate air containing infectious droplet nuclei. Because sites of potential transmission of tubercle bacilli are numerous and difficult to identify in advance, this strategy is used routinely only where the risk of transmission is known to be exceptionally high. Some of these areas include mycobacteriology laboratories, sputum induction cubicles, chest clinic waiting areas, and selected shelters for the homeless. To be effective, ventilation systems and ultraviolet lights must be properly maintained.
4. In the United States, BCG vaccination is recommended only for uninfected children who are at unavoidable risk of exposure to TB and for whom other methods of prevention and control have failed or are not feasible.

#### BCG VACCINES

BCG was derived from a strain of *M. bovis* attenuated through years of serial passage in culture by Calmette and Guérin at the Pasteur Institute in Lille, France. It was first administered to humans in 1921. Many BCG vaccines are available worldwide; all are derived from the original strain but vary in cultural characteristics and in ability to induce sensitization to tuberculin. BCG vaccines vary because of genetic changes in the bacterial strains and because of differences in techniques of production, in methods and routes of vaccine administration, and in characteristics of the populations and environments in which BCG vaccines have been studied.



Production standards for BCG vaccines, set by the Food and Drug Administration, specify that they be freeze-dried products containing live bacteria from a documented strain of BCG. The strain must demonstrate various specified characteristics of safety and potency in animals and induce tuberculin sensitivity in guinea pigs and humans. The vaccines currently available in the United States have been evaluated only for their ability to induce a delayed hypersensitivity state.

#### Vaccine Efficacy Studies

BCG vaccines vary substantially in efficacy. Different preparations of liquid BCG used in controlled community trials conducted before 1955 gave estimated efficacies ranging from -56% and 80% (21). In 1969, a large controlled trial was begun in Madras (Chingleput) in south India to estimate the efficacy of two strains of freeze-dried BCG vaccine at two different doses. After 15 years of follow-up, the risk of sputum-positive pulmonary TB in persons vaccinated with BCG was not lower than that in persons given placebo (22).

Although randomized controlled trials are the most reliable method for assessing vaccine efficacy, less precise estimates can be obtained more quickly and less expensively by observational studies (case-control, historical cohort, and cross-sectional studies) in areas where vaccination is performed at birth. Data from such studies show that the incidence of tuberculous meningitis and military TB is 52%–100% lower and that the incidence of pulmonary TB is 2%–80% lower in vaccinated children <15 years of age than in unvaccinated controls (1–4,23,24). However, because vaccination is not allocated randomly in observational studies, disproportionate exposure to TB may distort the estimates of vaccine efficacy.

#### Side Effects and Adverse Reactions

BCG rarely causes serious complications. Side effects vary by vaccine strain; they also vary for the same strain over time. Side effects occur in 1%–10% of vaccinated persons and usually include severe or prolonged ulceration at the vaccination site, lymphadenitis, and lupus vulgaris. The risk of side effects is greater with more potent vaccines. Some vaccine strains have caused osteomyelitis in one case per million doses administered. Disseminated BCG infection and death have occurred in one to 10 cases per 10 million doses administered, although this problem is restricted almost exclusively to persons with impaired immunity.

Data on adverse reactions may pertain to the vaccines licensed in the United States. The reported frequency of complications has varied, depending in part on the intensity of the surveillance effort.

In persons with tuberculous infections, the response to BCG vaccine is accelerated. This accelerated response is generally characterized by the appearance of induration >5 mm in diameter within 24–48 hours after vaccination, formation of a pustule within 5–7 days, and scab formation and healing in 10–15 days (25). The normal response to BCG vaccine begins 2–3 weeks after vaccination. Scar formation and healing occur within 3 months.

#### Interpretation of Tuberculin Test Following BCG Vaccination

The size of tuberculin skin test reactions caused by BCG vaccination (i.e., postvaccination sensitivity) varies by strain and dose of vaccine, age and nutritional status at vaccination, number of years since vaccination, and frequency of tuberculin testing. Mean size of skin test reactions in BCG-vaccinated children range from 3 mm to 19 mm (26–35). The presence or size of postvaccination tuberculin skin test reactions does not reliably predict the degree of protection afforded by BCG (36).

After BCG vaccination, it is usually not possible to distinguish between a tuberculin skin test reaction caused by virulent mycobacterial infection or by vaccination itself (37). Therefore, TB should be included in the differential diagnosis of any TB-like illness, especially if the person has been recently exposed to a person with infectious TB or received BCG several years before being tuberculin tested (38).

General guidelines exist for interpreting tuberculin skin test reactions in BCG vaccine recipients. The probability that a skin test reaction results from exposure to *M. tuberculosis* increases 1) as the size of the reaction increases, 2) when the patient is a contact of a person with TB, especially if that person has infected others, 3) when there is a family history of TB or when the patient's country of origin has a high TB prevalence, and 4) as the length of time between vaccination and tuberculin testing increases (38). For example, a positive skin test (>10 mm) usually can be attributed to *M. tuberculosis* infection if the vaccinated person is in a group at high risk for TB or has known exposure to a person with infectious TB. However, in vaccinated persons who do not belong to groups at high risk for infection and have no known exposure, a positive skin test reaction probably does *not* indicate recent infection with *M. tuberculosis*.

## GENERAL RECOMMENDATIONS

In the United States, the general population is at low risk for acquiring tuberculous infection. Furthermore, TB can be controlled successfully in most high-risk groups by modern methods of case detection, chemotherapy, and preventive therapy. In most population groups, prevention of TB is most reliably accomplished by periodic Mantoux testing with PPD tuberculin for high-risk children and adults and with administration of preventive therapy to those whose skin test reactions convert from negative to positive. Preventive chemotherapy should also be given to tuberculin-positive persons who are contacts of persons with infectious TB and to other high-risk tuberculin-positive persons (39). Therefore, a BCG vaccination policy for the entire population is not indicated. However, BCG vaccination may contribute to TB control in selected population groups. For example, it may benefit uninfected children who are at high risk for continuous or repeated exposure to infectious persons who remain undetected or untreated.

### Recommended Vaccine Recipients

**Exposed tuberculin skin-test-negative infants and children.** BCG vaccination is strongly recommended for infants and children with negative tuberculin skin tests who 1) are at high risk of intimate and prolonged exposure to persistently untreated or ineffectively treated patients with infectious pulmonary TB, cannot be removed from the source of exposure, and cannot be placed on long-term preventive therapy, or 2) are continuously exposed to persons with TB who have bacilli resistant to isoniazid and rifampin.

**Groups with an excessive rate of new infections.** BCG vaccination is also recommended for tuberculin-negative infants and children in groups in which the rate of new infections exceeds 1% per year (40) and for whom the usual surveillance and treatment programs have been attempted but are not operationally feasible. These groups include persons without regular access to health care, those for whom usual health care is culturally or socially unacceptable, or groups who have demonstrated an inability to effectively use existing accessible care.

### Discontinued Recommendation for Health-Care Workers

In the past, BCG vaccine was recommended for health-care workers, who as a group experienced high rates of new infection. However, BCG is *no longer recommended* for this group. Instead, health-care workers should be protected by adequate surveillance by periodic tuberculin skin testing (41) and isoniazid preventive therapy for all skin-test-positive health-care workers who are at high risk for developing disease. These persons include recent skin test converters and workers who are close contacts of TB patients or those who have medical conditions such as diabetes, renal failure, or immunosuppression associated with therapy or disease (39). In addition, hospital infection control measures, especially the prompt identification and implementation of precautions for patients with suspected TB, will help reduce the risk of TB transmission to health-care workers (42).

### Vaccine Availability

Two BCG vaccine strains licensed in the United States are available. The Glaxo strain is available from Quad Pharmaceuticals, Inc., Indianapolis. The Tice strain is available from Bionetics Research, Inc., Chicago, or Antigen Supply House, Northridge, California.

### Vaccine Dose and Administration

BCG should be reserved for persons whose skin test is negative to 5 tuberculin units of PPD tuberculin. The Glaxo strain is administered intradermally and the Tice strain percutaneously. Vaccination should be administered only by the route indicated in the package labeling and only in the suggested dose.

Infants <30 days old should receive one half the usual dose. If the indications for vaccination persist, they should receive a full dose at 1 year of age.

Freeze-dried vaccine should be reconstituted, protected from exposure to light, refrigerated when not in use, and used within 8 hours.

### Contraindications to Use

BCG should not be given to persons 1) whose immunologic responses are impaired because of congenital immunodeficiency, HIV infection, leukèmia, lymphoma, or generalized malignancy or 2) whose immunologic responses have been suppressed by steroids, alkylating agents, antimetabolites, or radiation.

BCG vaccine should be administered with caution to persons in groups at high risk for HIV infection. An AIDS patient was reported to have developed disseminated *M. bovis* disease after vaccination with

BCG (43). Three infants with symptomatic HIV infection were reported to have developed BCG adenitis after vaccination (44); however, disseminated BCG disease has not been reported in persons with asymptomatic HIV infection.

Theoretically, persons with asymptomatic HIV infection may be at greater risk for complications from BCG vaccine, but data are inconclusive regarding this elevated risk. The World Health Organization has recommended that in populations where the risk of tuberculosis is high, HIV-infected children who are asymptomatic should receive BCG vaccine at birth or as soon as possible thereafter. BCG vaccine should not be given to children with symptomatic HIV infection (45). In populations where the risk of TB is low, BCG vaccine should be withheld from persons known or suspected to be infected with HIV (45). The latter recommendation would apply to most populations in the United States for whom BCG might be considered.

#### Use in Pregnancy

Although harmful effects of BCG on the fetus have not been observed, women should avoid vaccination during pregnancy.

#### SURVEILLANCE

All suspected adverse reactions to BCG should be reported to the manufacturer and to the Office of Biologics Research, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland. These reactions occasionally occur >1 year after vaccination.

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Current Trends

**Prevention and Control of Tuberculosis  
in Correctional Institutions: Recommendations  
of the Advisory Committee for the Elimination of Tuberculosis**

*These recommendations are designed to assist federal, state, and local correctional officials in controlling tuberculosis (TB) among inmates and staff of correctional facilities (e.g., prisons, jails, juvenile detention centers). This document addresses issues unique to correctional institutions; more general information about TB is available in the official American Thoracic Society (ATS)/CDC statements referenced in this document.*

**BACKGROUND**

TB remains a problem in correctional institutions (1-8), where the environment is often conducive to airborne transmission of infection among inmates, staff, and visitors. In a survey of TB cases reported during 1984 and 1985 by 29 state health departments, the incidence of TB among inmates of correctional institutions was more than three times higher than that for nonincarcerated adults aged 15-64 years (CDC, unpublished data). Since 1985, 11 known TB outbreaks have been recognized in prisons in eight states (CDC, unpublished data). In addition, in some large correctional systems, the incidence of TB has increased dramatically. Among inmates of the New York State system, TB incidence increased from an annual average of 15.4 per 100,000 population during 1976-1978 to 105.5 per 100,000 in 1986 (1). In New Jersey during 1987, the incidence of TB among state inmates was 109.9 per 100,000—a rate 11 times that of the general population in New Jersey that year (New Jersey State Department of Health, unpublished data). In a survey of California Department of Corrections facilities, the TB incidence among inmates during 1987 was 80.3 per 100,000—a rate nearly six times that of California's general population for that year (California Department of Health Services, unpublished data).

Human immunodeficiency virus (HIV) infection among prisoners in a number of geographic areas heightens the need for TB control among inmates (9,10). According to a National Institute of Justice (NIJ) survey, as of October 1988, a cumulative total of 3136 confirmed acquired immunodeficiency syndrome (AIDS) cases had been reported among U.S. inmates since 1981—2047 cases by 44 of 51 state and federal systems and 1089 cases by 26 responding city and county jail systems. These

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES / PUBLIC HEALTH SERVICE

*TB - Continued*

reported AIDS cases represent a 60% increase since a similar survey was conducted in 1987. The incidence of AIDS among prisoners has been reported as markedly higher than that among the total U.S. population (9). During 1988, the incidence of AIDS in the U.S. population was 13.7 per 100,000 (11).<sup>\*</sup> During the same year, the estimated aggregate incidence for state/federal correctional systems was 75 cases per 100,000.<sup>†</sup> Rates for individual systems ranged from 0 to 536. Although more than half the states have rates  $\leq 25$ , eight state systems have rates  $\geq 100$ . The aggregate rate for 26 responding city/county jail systems was 183 per 100,000. However, rates in city/county jails were described by NIJ as "extremely suspect" because of rapid turnover of population (9).

HIV infection in persons with latent tuberculous infection appears to create a very high risk for development of TB (12-14). One review of AIDS cases among inmates in selected New York correctional facilities found TB in 22 (6.9%) of 319 persons with AIDS (3).

Transmission of TB in correctional facilities presents a health problem for the institutions and may also be a problem for the community into which inmates are released. Each year, more than 8 million inmates are discharged from local jails (15) and more than 200,000 from state and federal prisons (16). Because the median age of inmates on release is relatively young—27 years (17)—the total lifetime risk for TB in persons infected during incarceration is considerable.

**GENERAL GUIDELINES**

Control of TB is essential in correctional health care. Each correctional institution should designate an appropriately trained official responsible for operating a TB prevention and control program in the institution. A multi-institutional system should have a qualified official and unit to oversee TB-control activities throughout the system. These responsibilities should be specified in the official's job performance plan. The basic activities to be followed are surveillance, containment, and assessment.

**Surveillance** refers to identification and reporting of all TB cases in the system or institution and identification of all inmates and staff who are infected with TB (i.e., those with positive skin tests). New cases and newly infected persons must be quickly identified, and appropriate therapy begun.

**Containment** refers to ensuring that transmission of tuberculous infection does not occur. Appropriate diagnostic, treatment, prevention, and laboratory services must be available. Environmental factors conducive to the spread of TB, such as poor ventilation, should be corrected. Prison officials must ensure that persons undergoing treatment or preventive therapy be carefully monitored for compliance and drug toxicity and complete an appropriate course of treatment.

**Assessment** refers to prison officials' responsibility for knowing whether the surveillance and containment activities are being carried out effectively.

<sup>\*</sup>The incidence for the population at large was calculated as follows: (total number of cases reported to CDC in 1988 ÷ total population) x 100,000.

<sup>†</sup>Incidence for correctional inmates was approximated from a point prevalence as follows: (AIDS patients in the system at the time of the survey ÷ current inmate population of the system) x 100,000. Data on number of cases by year reported are not available for most correctional systems. The method used may underestimate the actual annual incidence in a correctional system.

TB - Continued  
SURVEILLANCE

Diagnosis

The intracutaneous Mantoux tuberculin test (not multiple puncture tests) should be used to identify persons infected with tubercle bacilli. Generally, for correctional institution staff and inmates, a tuberculin skin-test reaction  $\geq 10$  mm induration is considered positive. However, a reaction of  $\geq 5$  mm is considered positive in persons who have had close recent contact with an infectious person and in persons who have an abnormal chest radiograph consistent with TB (18). In addition, infected persons who are immunosuppressed for any reason may show little or no reaction to the tuberculin test (19). Therefore, a tuberculin skin-test reaction in a person known to be infected with HIV should be considered positive if induration is  $\geq 5$  mm (20).

Skin testing of inmates and staff should be carried out at entry or on employment, respectively (21). Each skin test should be administered and read by appropriately trained personnel and recorded in mm induration in the personal medical record. All inmates and staff should participate, except those providing documentation of a previous positive reaction to the tuberculin test.

*In jails with a rapid turnover of inmates, authorities may decide not to tuberculin test new detainees who are unlikely to remain in the system or in that facility for >7 days. However, provision must be made for appropriate diagnostic measures (e.g., sputum smear and culture and/or chest radiograph) for all persons who are symptomatic (18,20). (See Containment, below.)*

In most correctional institutions, skin-test-negative inmates and employees having contact with inmates should have repeat skin tests at least annually. If data from previous screening and TB casefinding are available, the frequency for repeat skin testing should be determined based on the need for timely surveillance information. Observed risk of new tuberculous infection is the most useful evaluation criterion to consider. In institutions with a historically low risk of tuberculous infection (e.g., <0.5% of persons with skin-test conversions annually), an increase in AIDS cases or TB cases should be viewed as indicating a need for more frequent skin testing and intensified TB casefinding activities.

Persons with positive skin-test reactions and all persons with symptoms suggesting TB (e.g., cough, anorexia, weight loss, fever) should receive a chest radiograph within 72 hours of skin-test reading or identification of symptoms. Correctional health-care personnel should be aware of the often atypical signs and symptoms of TB in persons with HIV infection (20). Inmates with abnormal chest radiographs and/or symptoms compatible with TB should also have sputum smear and culture examinations. Sputum should be submitted for smear and culture examination from persons with pneumonia or bronchitis symptoms that fail to abate promptly after initiation of antibiotic treatment. Three specimens should be collected, preferably once daily on 3 consecutive days. In the absence of spontaneous production of sputum, aerosol induction in a properly ventilated area should be used to obtain specimens.

Tuberculin skin-test energy may be a relatively late development in the progression from HIV infection to AIDS (22); consequently, inmates with known or suspected HIV infection (including those with nonreactive tuberculin tests) should receive a chest radiograph as part of initial screening, regardless of tuberculin skin-test status.

**TB - Continued****Case Reporting**

Whenever TB is suspected or confirmed among inmates or staff, this information should be immediately entered into the TB-control records at the institution and at the headquarters level, if in a multi-institutional system. The local or state health department should also be notified, as required by state and local laws or regulations.

**Contact Investigation**

Because TB is transmitted by the airborne route, persons at highest risk for acquiring infection are "close contacts" (e.g., persons who sleep, live, work, or otherwise share air with an infectious person through a common ventilation system). When a person with suspected or confirmed TB appears to be infectious (e.g., has pulmonary involvement on chest radiograph and cough, and/or positive sputum smear), close contacts must be skin tested unless they have a documented history of a positive tuberculin test (27). Close contacts with a positive tuberculin reaction or a history of a previous positive test and symptomatic persons, regardless of skin-test results, should receive immediate chest radiographs to detect evidence of pulmonary TB.

Depending on the ventilation in an institution, close contacts could include all cellmates, all inmates and staff on a tier, or all inmates and staff in a building. Health department staff should be consulted to determine who should be tested. When tuberculin converters are found among the close contacts, other persons with less contact may need to be examined. Every effort should be made by medical and nonmedical staff to ensure the confidentiality of persons with TB.

Close contacts with positive tuberculin reactions but without TB should be given at least 6 months' preventive therapy (see Preventive Therapy, below) unless medically contraindicated (27). Close contacts who do not have a positive tuberculin reaction and who are asymptomatic should have a repeat tuberculin test 10-12 weeks after contact has ended.

Contacts with known or suspected HIV infection should be considered for a 12-month course of preventive therapy, regardless of skin-test results, if evidence indicates that the source patient was infectious.

A patient with clinical TB may have negative sputum smears or cultures, especially if recently infected. Close contacts of such persons should also be examined to detect a source case and other newly infected inmates or staff.

**CONTAINMENT****Isolation**

Persons with suspected or confirmed TB who have pulmonary involvement on chest radiograph, cough, and/or a positive sputum smear should be immediately placed in respiratory isolation (e.g., housed in an area with separate ventilation to the outside, negative air pressure in relation to adjacent areas, and at least four to six room air exchanges per hour) (23). It may be necessary to move a patient to another facility or hospital with a respiratory isolation facility.

Respiratory isolation should continue until patients are on appropriate therapy and at least three consecutive daily negative sputum smears indicate that respiratory precautions may be removed. No special precautions are needed for handling patients' dishes, books, laundry, bedding, or other personal items.

Inadequate or interrupted treatment for TB can lead to drug-resistant TB and transmission of infection. Therefore, after effective medications have begun, it is of



*TB - Continued*

utmost importance to keep the patient on medication until completion of therapy, unless signs or symptoms of an adverse reaction appear. Arrangements must be made with the health department for continued medication and follow-up before an inmate with TB is released. Similar arrangements should be made before the release of inmates on preventive therapy.

Because crowding and poor ventilation are conducive to transmission of TB, improvements in housing conditions can help prevent outbreaks. Installing ultraviolet lights may be helpful in prisons where transmission of tuberculous infection has been a problem (24). Although the effectiveness of ultraviolet lights in decreasing TB transmission in such settings has not been confirmed by epidemiologic studies, ultraviolet lights have been used to reduce transmission of TB in hospitals and shelters for the homeless (23,25). When ultraviolet lights are used, proper installation and maintenance is essential (24).

**Treatment**

ATS/CDC recommendations should be followed for treatment and management of persons with confirmed or suspected TB (20,26). Each dose of medication should be administered by a designated ancillary medical staff person who watches the inmate swallow the pills. The medication may be given twice weekly (with appropriate change in dosage) after 1-2 months of daily medication (26). To ensure continuing compliance, if a patient is to be discharged before completion of therapy, the health department should be notified before the inmate is released.

Persons with positive smears or cultures at the beginning of therapy should be monitored by repeat sputum examinations for treatment response until they become smear-negative. Treatment failure is usually due to patient noncompliance with therapy but may be due to the presence of drug-resistant organisms.

All patients must be monitored by trained personnel for signs and symptoms of adverse reactions during chemotherapy (20,26). Expert medical consultation regarding monitoring and/or treatment of patients with complications (e.g., AIDS, drug resistance, adverse reactions, pregnancy, nonpulmonary TB) should be sought when necessary. Special emphasis should be placed on close supervision and care of TB patients infected with drug-resistant organisms.

Inmates with TB should be routinely offered testing with appropriate counseling for HIV infection. The presence of HIV infection necessitates longer treatment for TB and continued close observation for adverse drug reactions, treatment failure, and relapse (20).

**Preventive Therapy**

All inmates and staff with positive tuberculin reactions who have not previously completed an adequate course of preventive therapy should be considered for preventive therapy unless there are medical contraindications (20,26). Eligible inmates include those who will be incarcerated long enough to complete at least 1 month of continuous therapy; provisions should be made before release for the health department to oversee completion of at least 6 months of appropriate therapy (unless HIV infected; see below).

HIV-antibody testing should be offered to all known tuberculin-positive inmates. Tuberculin-positive persons with concurrent HIV infection appear to be at very high risk for TB and have highest priority for preventive therapy, regardless of age. Efforts should be made to encourage persons with known or suspected HIV infection to complete 12 months of therapy.

**TB -- Continued**

Each dose of preventive therapy should be administered by a designated ancillary medical staff person who watches the patient swallow the pills. Since daily supervised therapy is often not feasible, twice-weekly supervised therapy is a satisfactory alternative.

Most experts believe twice-weekly intermittent preventive therapy (using isoniazid [INH] 900 mg) is effective, although it has not been studied in controlled clinical trials. Medication should *not* be given to an inmate without direct observation of drug ingestion.

All persons on preventive therapy must be monitored by trained personnel for signs and symptoms of adverse reactions during the entire treatment period (26). Some prison inmates will have underlying liver disease related to previous alcohol or narcotic abuse (27-29). Although chronic liver disease is not a contraindication to INH preventive therapy, such patients should be carefully monitored (26).

Persons for whom TB preventive therapy is recommended but who refuse or are unable to complete a recommended course should be counselled to seek prompt medical attention if they develop signs or symptoms compatible with TB. Routine periodic chest radiographs are generally not useful for detecting disease in the absence of symptoms; chest radiographs should be reserved for persons with symptoms, especially a persistent cough.

**ASSESSMENT**

Inmates are transferred frequently. Thus, record systems for tracking and assessing the status of persons with TB and tuberculous infection in the prison facilities are essential. These systems must be maintained by using current information on the location, treatment status, and degree of infectiousness of these persons. Prompt action must be taken to assure reinstatement of drug therapy should treatment lapse for any reason.

The record systems should also provide data needed to assess the overall effectiveness of TB-control efforts, and the following information should be reviewed at least every 6 months:

1. Tuberculous infection prevalence and tuberculin conversion rates for inmates and staff within each institution;
2. Case numbers and case rates;
3. Percentage of TB patients recommended for therapy who complete the prescribed 6-month course of directly observed therapy in 6-9 months (goal is  $\geq 95\%$ );
4. Percentage of patients with culture-positive sputum that converts to culture negative within 3 months of starting treatment (goal is  $\geq 90\%$ );
5. Percentage of persons placed on INH preventive therapy who complete at least 6 months of directly observed therapy (goal is  $\geq 90\%$ ).

In multi-institutional systems, these data should be compiled for individual institutions and for the system as a whole, with results provided to corrections and health department officials.

**ROLE OF THE HEALTH DEPARTMENT**

Health departments should assist correctional institutions in developing and updating policies, procedures, and record systems for TB control. The health department should also provide access to expert TB medical consultation. A specific health department contact person should be designated to provide epidemiologic

*TB - Continued*

and management assistance to correctional facilities, and this responsibility should be an element in the designated person's job performance plan. This responsibility may require considerable initial onsite consultation and subsequent semiannual evaluation for correctional institutions.

Health department staff should assist in developing programs to train correctional institution staff (e.g., to perform, read, and record tuberculin skin tests; identify signs and symptoms of TB; initiate and observe therapy; monitor for side effects; collect diagnostic specimens; educate inmates; maintain record systems). Health or corrections departments may wish to grant certification to correctional staff completing this training.

Health departments should also provide consultation for contact examinations within correctional institutions and assure appropriate examinations for nonincarcerated contacts of persons with TB who are identified in these institutions.

In addition, health departments should cooperate with correctional staff in arranging continuing treatment for inmates released while receiving TB treatment or preventive therapy.

Health departments have a responsibility to maintain TB registries with updated medical information on all current TB cases within their jurisdictions, including those in correctional institutions. Records should be assessed quarterly, and necessary revisions in policies or procedures should be recommended. In addition, health departments should periodically assess the impact of correctional institution-acquired TB and tuberculous infection on the community as a whole.

Because inmates may have both TB and HIV infection, health department officials should assist correctional institutions in developing and implementing HIV prevention programs. Such programs include strategies to identify persons practicing high-risk behaviors, to counsel those infected with HIV, and to reduce high-risk behaviors among all inmates.

As circumstances change, these recommendations will be periodically revised. They are not intended to discourage new and innovative approaches for dealing with TB prevention and control in prisoners. The recommendations should be used instead to enhance the quality of medical care for persons in correctional institutions.

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## DEFINITIONS OF ABBREVIATIONS AND TERMS USED IN THIS PUBLICATION

|       |   |
|-------|---|
| ACIP  | Immunization Practices Advisory Committee               |
| AIDS  | Acquired immunodeficiency syndrome                      |
| CDC   | Centers for Disease Control                             |
| CNS   | Central nervous system                                  |
| CRS   | Congenital rubella syndrome                             |
| GBS   | Guillain-Barré syndrome                                 |
| H     | Hemagglutinin   |
| HB    | Hepatitis B   |
| HBIG  | Hepatitis B immune globulin                             |
| HBsAg | Hepatitis B surface antigen                             |
| HBV   | Hepatitis B virus                                       |
| HDCV  | Human diploid cell rabies vaccine                       |
| HRIG  | Human rabies immune globulin                            |
| ID    | Intradermal, intradermally                              |
| IG    | Immune globulin   |
| IM    | Intramuscular, intramuscularly                          |
| IPV   | Inactivated poliovirus vaccine                          |
| MMR   | Measles, mumps, rubella vaccine                         |
| N     | Neuraminidase   |
| OPV   | Oral poliovirus vaccine                                 |
| SC    | Subcutaneous, subcutaneously                            |
| Td    | Tetanus and diphtheria combined toxoids (for adult use) |
| TIG   | Tetanus immune globulin                                 |
| VZIG  | Varicella-zoster immune globulin                        |
| WHO   | World Health Organization                               |



*This statement on adult immunization is a supplement to the "General Recommendations on Immunizations" of the Immunization Practices Advisory Committee (ACIP) (1). It presents an overview of immunizations for adults and makes specific immunization recommendations. The statement provides information on vaccine-preventable diseases; indications for use of vaccines, toxoids, and immune globulins recommended for adults; and specific side effects, adverse reactions, precautions, and contraindications associated with use of these immunobiologics. It also gives immunization recommendations for adults in specific age groups and for those who have special immunization requirements because of occupation, lifestyle, travel, environmental situations, and health status.*

*This statement, a compendium of ACIP recommendations, will not be updated regularly. The ACIP periodically reviews individual immunization statements, and revised statements are published in the MMWR. The reader must use the detailed, up-to-date individual statements in conjunction with this compendium in order to keep abreast of current information.*

## INTRODUCTION

In general, immunization policies have been directed towards vaccinating infants, children, and adolescents. While immunization is a routine measure in pediatric practice, it is not usually routine in the practice of physicians who treat adults.

The widespread and successful implementation of childhood immunization programs has greatly reduced the occurrence of many vaccine-preventable diseases. However, successful childhood immunization alone will not necessarily eliminate specific disease problems. A substantial proportion of the remaining morbidity and mortality from vaccine-preventable diseases now occurs in older adolescents and adults. Persons who escaped natural infection or were not immunized with vaccines and toxoids against diphtheria, tetanus, measles, mumps, rubella, and poliomyelitis may be at risk of these diseases and their complications.

To reduce further the unnecessary occurrence of these vaccine-preventable diseases, all those who provide health care to older adolescents and adults should provide immunizations as a routine part of their practice. In addition, the epidemiology of other vaccine-preventable diseases (e.g., hepatitis B, rabies, influenza, and pneumococcal disease) indicates that individuals in certain age, occupational, environmental, and lifestyle groups and individuals who have special health problems are at increased risk of these illnesses and should be immunized. Travelers to some countries may be at increased risk of exposure to vaccine-preventable illnesses. Finally, foreign students, immigrants, and refugees may be susceptible to these diseases.

A systematic approach to immunization is necessary to ensure that every adult is appropriately protected against vaccine-preventable diseases. Every visit by an adult to a health-care provider should be an opportunity to provide this protection. Several factors need to be considered before any patient is vaccinated. These include the susceptibility of the patient, the risk of exposure to the disease, the risk from the disease, and the benefits and risks from the immunizing agent. Physicians should maintain detailed information about previous vaccinations received by each individual, including type of vaccination, date of receipt, and adverse events, if any, following vaccination. Information should also include the person's history of vaccine-preventable illnesses, occupation, and lifestyle. Vaccine histories ideally should be based on written documentation to ascertain whether vaccines and toxoids were administered at appropriate ages and at proper intervals. Close attention to factors such as military service and age may be helpful in determining whether any vaccines or toxoids are advisable for an individual. After the administration of any immunobiologic, the patient should be given written documentation of its receipt and information on which vaccines or toxoids will be needed in

the future. For this purpose an immunization record form such as the suggested form found in Appendix 1 should be used routinely.

The patient or responsible person should be given information on the risks of immunobiologics as well as their major benefits in preventing disease both in individuals and in the community. No formal, legally acceptable statement has been universally adopted for the private medical sector. Thus, the ACIP recommends that there be ample opportunity for questions before each immunization. CDC has developed "Important Information Statements" for use with federally purchased vaccines given in public health clinics. Practitioners may wish to consider these or similar materials for patients. Examples of "Important Information Statements" can be obtained from state and many local health departments.

Modern immunobiologics are extremely safe and effective, but not completely so. All immunobiologics have had adverse events reported after administration. These range from frequent, minor, local reactions to extremely rare, severe systemic illness, such as paralysis associated with oral poliovirus vaccine (OPV). It is frequently impossible to establish cause-and-effect relationships when untoward events occur after vaccination since temporal association alone does not necessarily indicate causation. To improve knowledge about adverse reactions, all temporally associated events severe enough to require the recipient to seek medical attention should be evaluated and reported in detail to local or state health officials and to the manufacturer of the immunobiologic.

General immunization considerations and recommendations are found in the ACIP statement "General Recommendations on Immunization" (7).

The following recommendations apply generally to individuals in the indicated groups. For more detailed information on immunobiologics, including indications, side effects, adverse reactions, precautions, contraindications, dosage, and route of administration, providers are urged to refer to the following section on individual immunobiologics, the ACIP statements on specific immunobiologics (Appendix 2), and the tables and appendices at the back of this supplement. Appendix 3 provides a list of vaccines, toxoids, and immune globulins available in the United States as of June 1984.

## Age Groups

The following text and Table 1 summarize the vaccines and toxoids recommended for most adults in the specific age groups. The reader is referred to the section on specific immunobiologics for essential information.

### *Adults 18-24 Years Old*

All young adults should complete a primary series of diphtheria and tetanus toxoids. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Those who have completed a primary series should receive a booster dose every 10 years. There is no need to repeat doses when the series schedule is delayed. The combined tetanus-diphtheria toxoids for adult use, Td, should be used to enhance protection against both diseases. Persons with unknown or uncertain histories of receiving tetanus or diphtheria toxoids should be considered unimmunized and should receive a full three-dose primary series of Td.

Young adults should also be immune to measles, rubella, and mumps. Persons are considered immune to measles and mumps if they have a dated record of vaccination with live vaccines on or after their first birthday, documentation of physician-diagnosed disease, or laboratory evidence of immunity. Persons vaccinated in the period 1963-1967 with inactivated-

measles-virus vaccine or with a measles vaccine of unknown type should be revaccinated with live-measles-virus vaccine to prevent measles disease or atypical measles syndrome if exposed to wild measles virus. Persons are considered immune to rubella only if they have a record of vaccination with rubella vaccine on or after their first birthday or laboratory evidence of immunity. The combined measles, mumps, rubella (MMR) vaccine is the vaccine of choice if recipients are likely to be susceptible to more than one of the three diseases. Persons lacking adequate documentation as noted above should be vaccinated.

#### ***Adults 25-64 Years Old***

All adults 25-64 years of age should complete a primary series of tetanus and diphtheria toxoids. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Those who have completed a primary series should receive a booster dose every 10 years. The combined toxoids for adult use, Td, should be used to enhance protection against both diseases. Persons with unknown or uncertain histories of receiving tetanus or diphtheria toxoids should be considered unimmunized and should receive a full three-dose primary series of Td.

Adults born in 1957 or later should receive measles vaccine unless they have a dated record of vaccination with live-measles vaccine on or after their first birthday, documentation of physician-diagnosed disease, or laboratory evidence of immunity. Adults born before 1957 can be considered immune to measles, since measles was a universal infection before measles vaccine became available. While most adults are likely to have been infected naturally with mumps, mumps vaccine may be given to adults, especially males, who are considered susceptible. Unless proof of vaccination with rubella vaccine or laboratory evidence of immunity is available, rubella vaccine is recommended for women of childbearing age and for other adults who may find themselves in places where rubella transmission is likely to occur, such as hospitals, all types of schools, and other places where young people are likely to congregate. The combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to more than one of these three diseases.

#### ***Adults 65 Years Old or Older***

All older adults should complete a primary series of tetanus and diphtheria toxoids. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Those who have completed a primary series should receive a booster dose every 10 years. The combined toxoids for adult use, Td, should be used to enhance protection against both diseases. Persons with unknown or uncertain histories of receiving tetanus or diphtheria toxoids should be considered unimmunized and should receive a full three-dose primary series of Td.

All older adults should receive influenza vaccine annually. They should also receive a single dose of pneumococcal polysaccharide vaccine.

### **Special Occupations**

Persons in specific occupations may be at increased risk of exposure to certain vaccine-preventable illnesses. Such persons may need selected vaccines and toxoids in addition to those routinely recommended for their age group. Table 2 provides a summary of immunobiologics recommended for various special occupational groups. The reader is referred to the section on specific immunobiologics for essential information.

### *Health-Related Occupations*

Medical, dental, laboratory, and other support personnel who may have contact with blood or blood products should be immune to hepatitis B virus (HBV) infection. The groups at highest risk for acquiring HBV infection and for whom HB vaccine is recommended include medical technicians, operating room staff, phlebotomists, physicians (particularly surgeons and pathologists), nurses (particularly intravenous-therapy nurses and nurses on oncology and dialysis units), dentists and oral surgeons, laboratory and blood-bank technicians, and emergency-room staff. Morticians and their assistants who have routine contact with blood and secretions are also at high risk of HBV infection. Selected staff of institutions for the mentally retarded may be at increased risk of HBV infection because of exposure to bites and contact with skin lesions, saliva, and other potentially infected secretions in addition to blood.

Among health-care personnel with frequent exposure to blood, the prevalence of serologic evidence of HBV infection is estimated to range between 10% and 30%. Since the cost effectiveness of serologic screening to detect susceptible individuals among health-care personnel depends on the prevalence of infection, each institution must decide whether serologic screening is cost effective. Vaccination of individuals who already have antibodies to HBV has not been shown to cause adverse effects.

The duration of protection from a three-dose series of HB vaccine or the need for booster doses has not yet been determined.

Transmission of rubella in health facilities (hospitals, physician or dentist offices, clinics, etc.) can disrupt hospital or office routines and cause considerable expense. Although no cases of congenital rubella syndrome (CRS) have been reported in association with rubella transmission in health facilities, therapeutic abortions have been sought by pregnant staff members following rubella infection (2). To prevent such situations, all medical, dental, laboratory, and other support health personnel, both male and female, who might be at risk of exposure to patients infected with rubella, or who might have contact with pregnant patients, should be immune. Rubella vaccine is recommended for all such personnel unless they have either proof of vaccination with rubella vaccine on or after their first birthday or laboratory evidence of immunity. Combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to measles and/or mumps as well as to rubella.

Measles transmission in health facilities can also be disruptive and costly. To prevent such situations, all health personnel born in 1957 or later who may have contact with patients infected with measles should be immune. Such persons can be considered immune only if they have documentation of having received live-measles vaccine on or after their first birthday, a record of physician-diagnosed measles, or laboratory evidence of immunity. Measles vaccine is recommended for all persons lacking such documentation. Combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to rubella and/or mumps as well as to measles. Adults born before 1957 can be considered immune to measles since measles was a universal infection before the availability of measles vaccine.

Poliovirus vaccine is not routinely recommended for persons older than high school age (18-19 years old). However, hospital personnel having close contact with patients who may be excreting wild polioviruses, and laboratory personnel handling specimens that may contain wild polioviruses, should have completed a primary series of poliovirus vaccine. For personnel who do not have proof of having completed a primary series, completion is recommended with inactivated poliovirus vaccine (IPV). IPV is preferred because there is a slightly increased risk in adults of vaccine-associated paralysis following receipt of OPV. In addition, since vaccine poliovirus may be excreted by OPV recipients for 30 or more days, the use of OPV increases the risk of acquiring vaccine-associated paralytic poliomyelitis among susceptible immunocompromised contacts and susceptible close contacts of OPV recipients.

Smallpox vaccination is indicated only for laboratory workers involved with orthopox viruses or in producing and testing smallpox vaccine. When indicated, smallpox vaccination should be given at least every 3 years.

Plague vaccine is indicated for laboratory personnel working with *Yersinia pestis* possibly resistant to antimicrobial agents and for persons performing *Y. pestis* aerosol experiments.

Preexposure rabies vaccination is indicated for laboratory workers directly involved with testing or isolating rabies virus.

### ***Veterinarians and Animal Handlers***

Veterinarians and animal handlers are at risk of rabies exposure because of occupational contact with both domestic and wild animals. They should receive preexposure rabies-vaccine prophylaxis with human diploid cell rabies vaccine (HDCV). Preexposure vaccination against rabies does *not* eliminate the need for additional therapy after exposure to rabies; it does, however, simplify postexposure therapy by eliminating the need for human rabies immune globulin (HRIG) and by decreasing the number of postexposure doses of vaccine needed. Persons at continued risk of frequent exposure should receive a booster dose of HDCV every 2 years or have their serum tested for rabies antibody every 2 years and, if the titer is inadequate (< 5 by the rapid fluorescent-focus inhibition test), receive a booster dose.

### ***Selected Field Personnel***

Plague vaccine is indicated for field personnel who cannot avoid regular exposure to potentially plague-infected wild rodents and rabbits and their fleas.

Preexposure rabies vaccine prophylaxis should be considered for field personnel who are likely to have contact with potentially rabid dogs, cats, skunks, raccoons, bats, or other wild-life species.

### ***Sewage Workers***

Sewage workers, as all other adults, should be adequately vaccinated against diphtheria and tetanus.

Poliovirus and typhoid vaccines and immune globulin are not routinely recommended for sewage workers.

## **Lifestyles**

Various lifestyles may increase the risk of exposure to certain vaccine-preventable illnesses. Persons with these lifestyles may require vaccines in addition to those routinely recommended for their age group. Table 2 provides a summary of the vaccines recommended.

### ***Homosexually Active Males***

Homosexually active males are at high risk of HBV infection. Between 35% and 80% have serologic evidence of HBV infection. Susceptible homosexual males should be vaccinated with HB vaccine as early as possible after they begin homosexual activity because they can be expected to acquire HBV infection at a rate of 10%-20% per year. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined. Because of the high prevalence of infection, prevaccination serologic screening of homosexual males may be cost effective regardless of their age or of how long they have been homosexually active.

### ***Users of Illicit Injectable Drugs***

Users of illicit injectable drugs are at high risk of HBV infection. Serologic evidence of HBV infection has been found in 60%-80% of these individuals. Efforts should be made to vaccinate susceptible users with HB vaccine as early as possible after their drug use begins because they can be expected to acquire HBV infection at a rate of 10%-20% per year. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined. Because of the high prevalence of infection, prevaccination serologic screening of users of illicit injectable drugs to avoid unnecessary immunization is cost effective.

These drug users are also at increased risk of tetanus, and their tetanus immunization status should be kept up to date with Td.

### **Environmental Situations**

Certain environments may place an individual at increased risk of certain vaccine-preventable diseases. Table 2 summarizes additional vaccines recommended for persons in selected environments. The reader is referred to the section on specific immunobiologics for essential information.

#### ***Inmates of Long-Term Correctional Facilities***

Serologic evidence of HBV infection has been found in 10%-80% of male prisoners. Although the frequency of transmission during imprisonment has not been documented, the environment of long-term correctional facilities may be associated with a high risk of transmission of HBV infection because of the frequency of use of illicit injectable drugs and of homosexual behavior. In selected long-term institutional settings, prison officials may elect to undertake serologic HBV screening and vaccination programs. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

#### ***Residents of Institutions for the Mentally Retarded***

Institutions for the mentally retarded provide a setting conducive to the transmission of HBV infection through bites and contact with blood, skin lesions, saliva, and other potentially infectious secretions. Serologic evidence of HBV infection has been found in 35%-80% of residents of such institutions. New admissions to these institutions should be vaccinated as soon as possible. For current residents, screening and vaccination of susceptible residents is recommended. Because of the high prevalence of infection, preimmunization serologic screening of those already institutionalized may be cost effective; however, screening of new admissions very likely will not be. Residents of group homes, foster homes, and similar settings who have household contact with a carrier of HBV should also be vaccinated. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

### **Travel**

The risk of acquiring illness during international travel depends on the areas of the world to be visited and the extent to which the traveler is likely to be exposed to vaccine-preventable diseases. When considering travel, people often seek advice from health-care personnel on immunization. This provides a good opportunity to review the person's immunization status and administer primary series or booster doses, if needed.



In most countries, measles, mumps, and rubella remain uncontrolled. Therefore, the risk of acquiring these diseases while traveling outside the United States is greater than the risk incurred within the United States. Approximately 50% of imported measles cases reported for 1980-1983 occurred in citizens returning to the United States (3). To minimize importations by U.S. citizens, all travelers born in 1957 or later should be immune to measles. Women travelers of childbearing ages should be immune to rubella before leaving the United States.

In developed countries such as Japan, Canada, Australia, New Zealand, and the European countries, the risk of acquiring other vaccine-preventable diseases such as poliomyelitis, diphtheria, and tetanus is usually no greater than the risk incurred while traveling in the United States. In contrast, travelers to developing countries are, in general, at increased risk of exposure to many infections, including wild polioviruses and diphtheria. Accordingly, such travelers should be immune to poliomyelitis and diphtheria, in particular.

For protection against poliomyelitis, unimmunized adults should receive at least two doses of IPV 1 month apart, and preferably a complete primary series, before traveling to a developing country. If an individual's travel plans do not permit this interval, then a single dose of OPV is recommended. For adults previously incompletely immunized with OPV or IPV, the remaining doses of either vaccine required for completion of the primary series should be given, regardless of the interval since the last dose or the type of vaccine previously received. A single additional dose of either OPV or IPV should be given to travelers who have previously completed a primary series of OPV or IPV.

Selective immunization of travelers with vaccines against yellow fever, cholera, typhoid, plague, meningococcal disease, rabies, or HBV infection or administration of immune globulin (IG) to prevent hepatitis A is recommended on the basis of known, or perceived, disease-specific risks in the country(ies) to be visited and the type and duration of travel within a country. In the instances of cholera and yellow fever, vaccination requirements may have been established by the country to be visited. Countries currently reporting yellow fever, cholera, and plague are identified biweekly in the *Summary of Health Information for International Travel*, and information on known or probably infected areas is published annually in *Health Information for International Travel*, which also lists specific requirements for cholera and yellow fever vaccinations for each country. All state health departments and many county and city health departments receive both publications. For entry into countries requiring yellow fever or cholera vaccination, travelers must have an International Certificate of Vaccination validated by an appropriate authority. State or local health departments can provide the addresses of persons or centers able to validate certificates.

More information on specific vaccine-preventable illnesses that a traveler might encounter is provided in the sections describing specific vaccines.

## Foreign Students, Immigrants, and Refugees

In many countries children and adolescents are not routinely immunized against diphtheria, tetanus, measles, mumps, rubella, and poliomyelitis. As a result, persons entering the United States to pursue college and postgraduate studies or as immigrants or refugees may be susceptible to one or more of these diseases.

Unless foreign students, immigrants, and refugees can provide a vaccination record documenting the receipt of recommended vaccines or toxoids at appropriate ages and intervals or laboratory evidence of immunity, they should receive the appropriate vaccines for their age as noted in age-specific recommendations (see page 2S) and in Table 1. Poliovirus vaccines are not recommended, in general, for persons 18 years of age or older.

## Special Health Status

Some vaccines may be contraindicated for persons with certain health problems; other vaccines may be indicated because of an underlying health condition. Table 3 provides a summary of immunobiologics indicated or contraindicated for persons with selected health problems.

### *Pregnancy*

When any vaccine or toxoid is to be given during pregnancy, waiting until the second or third trimester, when possible, is a reasonable precaution to minimize concern about possible teratogenicity.

Pregnant women not vaccinated previously against tetanus and diphtheria should receive two doses of Td properly spaced. Those who have previously received one or two doses of tetanus or diphtheria toxoid should complete their primary series during pregnancy. A primary series is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. Pregnant women who have completed a primary series should receive a booster dose of Td if 10 or more years have elapsed since their last dose.

Because of a theoretical risk to the developing fetus, live-virus vaccines should not usually be given to pregnant women or to those likely to become pregnant within 3 months. If, however, immediate protection against poliomyelitis or yellow fever is needed because of imminent exposure, OPV or yellow fever vaccine may be given. If the only reason to vaccinate a pregnant woman with yellow fever vaccine is an international travel requirement, efforts should be made to obtain a waiver letter (see page 19S).

It is strongly recommended that rubella vaccine be administered in the postpartum period to women not known to be immune, preferably before discharge from the hospital.

Information about immunobiologics and vaccine-preventable diseases during pregnancy is summarized in Appendix 4.

### *Conditions That Compromise the Immune System*

Persons with conditions that compromise their immune responses (e.g., leukemia, lymphoma, and generalized malignancy or immunosuppressive therapies) should receive annual influenza vaccination with the currently formulated vaccine. Persons with conditions associated with increased risk of pneumococcal disease or its complications should receive a single dose of pneumococcal polysaccharide vaccine. The effectiveness of these vaccines in such persons may be limited, but the risk of disease is substantial and adverse reactions are minimal.

In general, live-virus vaccines should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. However, susceptible patients with leukemia in remission who have not had chemotherapy for at least 3 months may receive live-virus vaccines. The exact interval between discontinuing immunosuppressives and regaining the ability to respond to individual vaccines is not known. Estimates of experts vary from 3 months to 1 year.

Short-term (less than 2 weeks) corticosteroid therapy, topical steroid therapy (e.g., nasal or skin), and intraarticular, bursal, or tendon injections with corticosteroids should not be immunosuppressive and do not necessarily contraindicate vaccination with live-virus vaccines. Vaccination should be avoided if systemic immunosuppressive levels are achieved by topical application.

### ***Hemodialysis***

Persons receiving hemodialysis have been at high risk of infection with HBV, although environmental control measures have reduced this risk during the past few years. Nationwide, an estimated 15% of hemodialysis patients have serologic evidence of HBV infection, and routine serologic screening of hemodialysis patients is currently recommended. Susceptible patients who will soon require or are currently receiving long-term hemodialysis should receive three double doses of HB vaccine as soon as possible. Double the normal dose is recommended for these patients because of lower vaccine immunogenicity in this group. Postvaccination screening to demonstrate antibody to hepatitis B surface antigen (HBsAg) is recommended in this group. Approximately 60% of hemodialysis patients who receive double doses of HB vaccine demonstrate antibodies against HBV. The duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

Because persons with chronic renal disease are at increased risk of adverse consequences from infections of the lower respiratory tract, hemodialysis patients should receive annual influenza vaccination with the current formulated vaccine. These patients are also at increased risk of developing pneumococcal infection, as well as of experiencing more severe pneumococcal disease, and should receive pneumococcal polysaccharide vaccine.

### ***Splenic Dysfunction or Anatomic Asplenia***

Persons with splenic dysfunction or anatomic asplenia are known to be at increased risk of contracting fatal pneumococcal bacteremia and should receive pneumococcal polysaccharide vaccine. Persons scheduled for elective splenectomy should receive pneumococcal polysaccharide vaccine at least 2 weeks before the operation.

### ***Factor VIII and IX Deficiencies***

Patients with clotting disorders who receive factor VIII or IX concentrates have an increased risk of HBV infection. Vaccination with HB vaccine is recommended for susceptible patients. The degree and duration of protection from a three-dose series of HB vaccine and the need for booster doses have not yet been determined.

Prevaccination serologic screening for HBV markers is recommended for patients who have already received multiple infusions of these products.

### ***Chronic Alcoholism***

Persons with chronic alcoholism may be at increased risk of contracting a pneumococcal infection or having a more severe pneumococcal illness. Such persons, especially those with cirrhosis, should receive pneumococcal polysaccharide vaccine.

### ***High-Risk Diseases***

Persons with disease conditions that increase the risk of adverse consequences from lower-respiratory-tract infections should receive annual influenza vaccination with the current formulated vaccine. These conditions include:

- (a) Acquired or congenital heart disease with actual or potentially altered circulatory dynamics.
- (b) Any chronic disorder or condition that compromises pulmonary function.
- (c) Diabetes mellitus or other metabolic diseases that increase the likelihood that infections will be more severe than for persons without such conditions.

(d) Chronic renal disease with azotemia or nephrotic syndrome.

(e) Chronic, severe anemia, such as sickle cell disease.

Some chronic illnesses (e.g., chronic pulmonary disease, congestive heart failure, diabetes mellitus) predispose individuals to an increased risk of pneumococcal illness or its complications. While data on the effectiveness of pneumococcal polysaccharide vaccine for chronically ill persons are not conclusive, such persons should receive the vaccine.

## VACCINE-PREVENTABLE DISEASES AND THEIR IMMUNOBIOLOGICS

Vaccines, toxoids, and immune globulins are available for use in the prevention of a number of diseases. These diseases and their specific immunobiologics are presented in this section. For each immunobiologic, dosage, route of delivery, indications for use, side effects, adverse reactions, precautions, and contraindications to be considered before administration are described here and are summarized in Table 4.

### Toxoids

#### *Diphtheria*

The occurrence of diphtheria has decreased dramatically in the United States, largely because of the widespread use of diphtheria toxoid. Only 11 cases of diphtheria were reported in the period 1980-1982. From 1977 through 1982, 56% of the 34 reported cases of respiratory diphtheria occurred in adults 20 years of age or older, and 24% of the cases occurred in adults 50 years of age or older. The age distribution for persons who died from diphtheria was similar. Diphtheria occurs primarily among unimmunized or inadequately immunized individuals. Limited serosurveys done since 1977 indicated that 62% of adults 18-39 years of age and 41%-84% of those 60 years of age or older lacked protective levels of circulating antitoxin against diphtheria (4-6).

- **Diphtheria toxoid**

Complete and appropriately timed immunization is at least 95% effective in preventing diphtheria. The combined preparation Td is recommended for use in adults since a large proportion of adults lack protective levels of circulating antibody against tetanus (4-6). Furthermore, Td contains much less diphtheria toxoid than other diphtheria toxoid-containing products, and as a result, reactions to the diphtheria component are less likely. Immunization with toxoid does not, however, prevent or eliminate carriage of *Corynebacterium diphtheriae*.

- **Toxoid indications**

All adults lacking a completed primary series of tetanus and diphtheria toxoids should complete the series with Td. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. All adults for whom 10 years or more have elapsed since completion of their primary series or since their last booster dose should receive a dose of Td. Thereafter, a booster dose of Td should be administered every 10 years. There is no need to repeat doses if the schedule for the primary series or booster doses is delayed. (For toxoid side effects and adverse reactions, and precautions and contraindications, see page 12S).

#### *Tetanus*

The occurrence of tetanus has decreased dramatically, largely because of the widespread use of tetanus toxoid. Nevertheless, the number of cases remained relatively constant from

1973 through 1982, averaging 88 reported cases per year. Tetanus occurs almost exclusively in unimmunized or inadequately immunized individuals. Immune pregnant women confer temporary protection against tetanus to their infants through transplacental maternal antibody. In the period 1977-1982, persons 20 years of age or older accounted for 89% of the 504 reported tetanus cases for which patient ages were known; persons 60 years of age or older accounted for 55%. The age distribution of persons who died from tetanus was similar. Serosurveys done since 1977 indicated that 11% of adults 18-39 years of age and 49% of those 60 years of age or older lacked protective levels of circulating antitoxin against tetanus (4-6).

- **Tetanus toxoid**

Complete and appropriately timed immunization is nearly 100% effective in preventing tetanus. The combined preparation, Td, is the preferred preparation for active tetanus immunization of adults since a large proportion of adults lack protective levels of circulating antitoxin against diphtheria (4-6).

- **Toxoid indications**

All adults lacking a complete primary series of tetanus and diphtheria toxoids should complete the series with Td. A primary series for adults is three doses of preparations containing tetanus and diphtheria toxoids, with the first two doses given at least 4 weeks apart and the third dose given 6-12 months after the second. All adults for whom 10 years or more have elapsed since completion of their primary series or since their last booster dose should receive a booster dose of Td. Thereafter, a booster dose of Td should be administered every 10 years. There is no need to repeat doses if the primary schedule for the series or booster doses is delayed.

The recommended pediatric schedule for DTP vaccine includes a booster dose at age 4-6 years. The first Td booster is recommended at age 14-16 years (10 years after the dose at age 4-6 years). One means of ensuring that persons continue to receive boosters every 10 years is to vaccinate persons routinely at mid-decade ages, e.g., 25 years, 35 years, etc.

For wound management the need for active immunization, with or without passive immunization, depends on the condition of the wound and the patient's immunization history. A summary of the indications for active and passive immunization is provided in Table 5. Only rarely have cases of tetanus occurred in persons with a documented primary series of toxoid injections.

Evidence indicates that complete primary immunization with tetanus toxoid provides long-lasting protection—10 years or more in most recipients. Consequently, after complete primary tetanus immunization, boosters are recommended at 10-year intervals. For clean and minor wounds occurring during the 10-year interval no additional booster is recommended. For other wounds, a booster is appropriate if the patient has not received tetanus toxoid within the preceding 5 years. Antitoxin antibodies develop rapidly in persons who have previously received at least two doses of tetanus toxoid.

Persons who have not completed a full primary series of injections or whose immunization status is unknown or uncertain may require tetanus toxoid and passive immunization at the time of wound cleaning and debridement. It is not sufficient to ascertain the interval since the most recent toxoid dose. A careful attempt should be made to determine whether a patient has previously completed primary immunization and, if not, how many doses have been given. Persons with unknown or uncertain previous immunization histories should be considered to have had no previous tetanus toxoid doses.

Td is the preferred preparation for active tetanus immunization in managing the wounds of adults. Td is used to enhance protection against diphtheria concurrently, since a large propor-

tion of adults are susceptible. Thus, if advantage is taken of visits for care of acute health problems, such as for wound management, some patients who otherwise would remain susceptible can be protected against both diseases. Primary immunization should ultimately be completed for persons documented to have received fewer than the recommended number of doses, including doses given as part of wound management.

If passive immunization is needed, human tetanus immune globulin (TIG) is the product of choice. The currently recommended prophylactic dose of TIG for wounds of average severity is 250 units, intramuscularly (IM). When tetanus toxoid and TIG are given concurrently, separate syringes and separate sites should be used. Most experts consider the use of adsorbed toxoid mandatory in this situation.

### ***Toxoid (Td) Side Effects and Adverse Reactions***

Local reactions, generally erythema and induration with or without tenderness, can occur after the administration of Td. Fever and other systemic symptoms are less common.

Arthus-type hypersensitivity reactions characterized by severe local reactions generally starting 2-8 hours after an injection and often associated with fever and malaise may occur, particularly in persons who have received multiple boosters of tetanus toxoid.

Rarely, severe systemic reactions such as generalized urticaria, anaphylaxis, or neurologic complications have been reported after administration of tetanus and diphtheria toxoids. Peripheral neuropathy has been reported rarely after administration of tetanus toxoid, although a causal relationship has not been established.

### ***Toxoid (Td) Precautions and Contraindications***

Although there is no evidence that tetanus and diphtheria toxoids are teratogenic, waiting until the second trimester of pregnancy to administer Td is a reasonable precaution to minimize any concern over teratogenicity.

A history of a neurologic reaction or a severe hypersensitivity reaction (e.g., generalized urticaria or anaphylaxis) following a previous dose is a contraindication to tetanus and diphtheria toxoids. Local side effects alone do not preclude continued use. If a prior systemic reaction is suspected of representing allergic hypersensitivity, appropriate skin testing to document immediate hypersensitivity may be useful before tetanus toxoid immunization is discontinued (7). Mild, nonspecific skin-test reactivity to tetanus toxoid is common. Most vaccinees develop cutaneous delayed hypersensitivity to the toxoid.

Persons experiencing severe Arthus-type hypersensitivity reactions to a prior dose of tetanus toxoid usually have very high serum tetanus antitoxin levels and should not be given even emergency booster doses of Td more frequently than every 10 years.

Although a minor illness, such as a mild upper-respiratory infection, should not be cause for postponing vaccination, a severe febrile illness is reason to defer routine vaccination.

## **Live-Virus Vaccines**

### ***Measles***

In 1983, only 5.6% of the 3,139 counties in the United States reported cases of measles. Indigenous transmission of measles has been eliminated from most of the United States because of widespread vaccination. However, importations of disease are frequent (more than 100 each year), and there is a continued risk of exposure, particularly for young adults attending college or universities or traveling abroad.

In 1982, 11.7% of measles patients whose ages were reported were 20 years of age or older. Outbreaks continue to occur in universities and colleges and other places where young

adults congregate. In the first half of 1983, 51% of reported cases were among college students or were epidemiologically linked to campus outbreaks. It is estimated that as many as 20% of young adults lack detectable antibody and may be susceptible to measles.

Encephalitis or death follows measles disease in approximately one case per 1,000. The risk of encephalitis is greatest in adult patients. Aside from infants, the highest measles case-fatality ratio occurs in adults.

Measles illness during pregnancy increases rates of spontaneous abortion, premature labor, and low birth weight for infants. Although cases of congenital malformation following measles infection during pregnancy have been reported, no consistent patterns have been demonstrated.

- **Measles vaccine**

Measles vaccine produces a mild or inapparent noncommunicable infection. A single subcutaneously (SC) administered dose of live-measles vaccine provides durable protection against measles illness in approximately 95% of vaccinees, extending probably for their lifetime. Combined MMR vaccine is the vaccine of choice if recipients are likely to be susceptible to rubella and/or mumps as well as to measles. Although reactions following measles, mumps, and rubella vaccines in persons previously immune have been reported, evidence and experience overwhelmingly suggest that vaccination with MMR of persons who were previously immune to one or more of its components is not associated with significant adverse effects.

- **Vaccine indications**

Measles vaccine is indicated for all persons born in 1957 or later who lack documentation of receipt of live-measles vaccine on or after their first birthday, physician-diagnosed measles, or laboratory evidence of immunity. Persons born before 1957 can generally be considered immune since measles was a universal infection before measles vaccine became available. Individuals who received vaccine before their first birthday, killed-measles vaccine, killed-measles vaccine followed within 3 months by live-measles vaccine, or a measles vaccine of unknown type in the period 1963-1967 should be revaccinated. An estimated 600,000-900,000 persons in the United States received killed-measles vaccine in the years 1963-1967.

Because the risk of acquiring measles outside the United States is greater than the risk incurred in the United States, travelers should be immune to measles before leaving the United States.

Generally, young adults who are exposed to measles and who have no or uncertain documentation of live-measles vaccination on or after their first birthday, no record of physician-diagnosed measles, and no laboratory evidence of immunity should be vaccinated within 72 hours after exposure, when vaccination is most likely to be protective. If the exposure did not result in infection, the vaccine should induce protection against subsequent measles infection. An acceptable alternative is to use IG, which can prevent or modify infection if administered within 6 days after exposure. IG is principally indicated when measles vaccine is contraindicated. IG should not be used in an attempt to control measles outbreaks. The recommended dose of IG is 0.25 ml/kg IM, not to exceed 15 ml. Live-measles vaccine should be given 3 months after IG is administered, by which time the passive measles antibodies should have disappeared.

- **Vaccine side effects and adverse reactions**

Reactions to measles vaccine do not appear to be age related. About 5%-15% of vaccinees may develop a temperature of 103°F (39.4°C) or higher, generally beginning between days 5 and 12 after vaccination; fever usually lasts 1-2 days and, rarely, up to 5 days. Transient

rashes have been reported in approximately 5% of vaccinees. The incidence rate of encephalitis or encephalopathy following measles vaccination is lower than the observed background incidence rate of encephalitis of unknown etiology and much lower than that following natural measles.

Reactions after live-measles vaccination occur in 4%-55% of prior recipients of killed-measles vaccine. The reactions are generally mild, consisting of a local reaction with or without a low-grade fever of 1-2 days' duration. Such reactions are considerably milder than atypical measles syndrome, an illness which may affect prior recipients of killed-measles vaccine who are exposed to natural measles.

- **Vaccine precautions and contraindications**

Vaccination should not be postponed because of a minor illness, such as a mild upper-respiratory infection. However, vaccination of persons with severe febrile illnesses should be postponed until recovery. Vaccine should be given 14 days before or deferred for at least 6 weeks, and preferably 3 months, after a person has received IG, whole blood, or other blood products containing antibody.

Because of a theoretical risk to the developing fetus, measles vaccine should not be given to pregnant women.

Measles vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

There is no evidence that live-measles vaccine exacerbates tuberculosis. If tuberculin skin testing is needed, it should be done on the day of vaccination and read 48-72 hours later. For a recent vaccinee, it is prudent to wait 4-6 weeks after receipt of measles vaccine before administering a tuberculin skin test since measles vaccination may temporarily suppress tuberculin reactivity.

Persons with a history of any sign or symptom of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) following ingestion of eggs or receipt of neomycin should be given measles vaccine only with extreme caution. Protocols have been developed for vaccinating such persons (8). Persons with reactions that are not anaphylactic are not at increased risk and can be vaccinated.

## ***Mumps***

The occurrence of reported mumps cases in the United States has decreased steadily since the introduction of live-mumps-virus vaccine. In 1983, a record low of 3,297 cases were reported provisionally; this number represented a 98% decline from the 185,691 cases reported in 1967, the year live-mumps vaccine was licensed. In 1982, 5,270 cases were reported, of which 9% occurred in persons 20 years of age or older.

Although mumps disease is generally self-limiting, meningeal signs may appear in up to 15% of cases, and orchitis in up to 20% of clinical cases among postpubertal males. Sterility is a rare sequela of mumps orchitis among males. Deafness occurs at a rate of one case per 15,000 cases of mumps.

Serologic surveys indicate that most individuals have been infected with mumps by 20 years of age.

- **Mumps vaccine**

Live-mumps vaccine has been available since 1967. A single dose of live-mumps vaccine administered SC provides protective and long-lasting levels of antibody in over 90% of recipients. Reported clinical vaccine efficacy ranges between 75% and 90%. MMR is the vaccine



of choice if recipients are likely to be susceptible to measles and/or rubella as well as to mumps. Although reactions following measles, mumps, and rubella vaccines in persons previously immune have been reported, evidence and experience overwhelmingly suggest that the vaccination with MMR of persons who were previously immune to one or more of its components is not associated with significant adverse effects.

- **Vaccine indications**

Mumps vaccine is indicated for all adults, particularly males, believed to be susceptible. Most adults are likely to have been infected naturally and generally can be considered immune, even if they did not have clinically recognizable mumps disease. Killed-mumps vaccine was available from 1950 until 1978. Persons who received killed-mumps vaccine might benefit from vaccination with live-mumps vaccine.

- **Vaccine side effects and adverse reactions**

Parotitis after vaccination has been reported rarely. Allergic reactions including rash, pruritus, and purpura have been associated temporally with mumps vaccination but are uncommon, usually mild, and of brief duration. The frequency of reported central nervous system (CNS) dysfunction following mumps vaccination is lower than the observed background incidence rate in the general population.

- **Vaccine precautions and contraindications**

Vaccine should be given at least 14 days before or deferred for at least 6 weeks, and preferably 3 months, after a person has received IG, whole blood, or other blood products containing antibody.

Because of the theoretical risk of fetal damage following administration of a live-virus vaccine to a pregnant woman, it is prudent to avoid giving mumps vaccine to pregnant women.

Mumps vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

Persons with a history of any sign or symptom of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) following ingestion of eggs or receipt of neomycin should be vaccinated only with extreme caution. Protocols have been developed for vaccinating persons with severe egg allergy (8). Persons with reactions that are not anaphylactic are not at increased risk and can be vaccinated.

## ***Rubella***

Preventing fetal infection and consequent CRS are the objectives of rubella immunization. Fetal infection occurring during the first trimester of pregnancy can lead to CRS in up to 80% of fetuses. In addition, fetal wastage due to miscarriage or therapeutic abortion following maternal rubella disease or exposure during the first trimester remains a frequent occurrence.

The number of reported rubella cases has decreased steadily from over 56,000 cases in 1969, the year rubella vaccine was licensed, to 2,325 cases in 1982. In 1982, only 11.7% of the 3,137 counties in the United States reported cases of rubella. The 1983 provisional total of 954 cases is an all-time low. Because, until recently, many adolescents and young adults had not been vaccinated, decreases in incidence rates of reported rubella were observed primarily for children. Recent efforts to increase delivery of vaccine to college-age and older persons have led to the current decline in the incidence rates for these age groups. However, an estimated 10%-15% of young adults remain susceptible to rubella, and limited outbreaks continue to be reported in universities, colleges, and places of employment—notably hospitals.

Vaccination of young children has prevented widespread epidemics of rubella and of CRS and eventually will lead to the elimination of CRS as vaccinated cohorts enter the childbearing age. However, increased efforts to ensure that all women of childbearing age, in particular, are vaccinated will hasten the elimination of rubella and CRS in the United States. Additional aids to elimination of rubella and CRS include 1) achieving and maintaining high immunization levels, 2) maintaining vigorous surveillance, and 3) practicing aggressive outbreak control.

- **Rubella vaccine**

A single SC administered dose of live, attenuated rubella vaccine provides long-term, probably lifetime, immunity in approximately 95% of vaccinees. Moreover, there is no risk to susceptible contacts of vaccinees. MMR is the vaccine of choice if recipients are likely to be susceptible to measles and/or mumps as well as to rubella. Although reactions following administration of measles, mumps, and rubella vaccines to persons previously immune have been reported, evidence and experience overwhelmingly suggest that the vaccination with MMR of persons who are already immune to one or more of its components is not associated with significant adverse effects.

- **Vaccine indications**

Rubella vaccine is recommended for adults, particularly females, unless proof of immunity is available (i.e., documented rubella vaccination on or after the first birthday or a positive serologic test) or unless the vaccine is specifically contraindicated. In particular, nonpregnant susceptible women of childbearing age should be provided rubella vaccination 1) during routine internal medicine and gynecologic outpatient care, 2) during routine care in a family planning clinic, 3) following premarital screening, 4) before discharge from a hospital for any reason, and 5) after childbirth or abortion. Ideally, any contact with the health-care system should be used as an opportunity to vaccinate susceptible women. In addition, evidence of rubella immunity should be required for all individuals in colleges and universities. Health-care programs in work places and in other places where women of childbearing age congregate should ensure that the rubella immune status of every employee is ascertained and that rubella immunization is made available. All hospital personnel (male and female) who might be at risk of exposure to patients infected with rubella or who might have contact with pregnant patients or personnel should be immune to rubella. Consideration should be given to making rubella immunity a condition for employment. Finally, since the risk of acquiring rubella while traveling outside the United States is greater than the risk incurred within the United States, all women travelers, particularly those of childbearing age, should be immune before leaving the United States.

- **Vaccine side effects and adverse reactions**

Up to 40% of susceptible adult vaccinees in large-scale field trials have had joint pain, usually of the small peripheral joints, after vaccination; frank arthritis is reported infrequently. Arthralgia and transient arthritis occur more frequently and tend to be more severe in susceptible women than in children. When joint symptoms or other types of pain and paresthesias do occur, they generally begin 3-25 days after vaccination, persist for 1-11 days, and rarely recur. Adults with joint problems usually have not had to disrupt work activities. Complaints of transient peripheral neuritis such as paresthesias and pain in the arms and legs have occurred very rarely and only in susceptible vaccinees.

- **Vaccine precautions and contraindications**

Rubella vaccine should be given at least 14 days before administration of IG or deferred for at least 6 weeks, and preferably 3 months, after administration. On the other hand, previous administration of whole blood or other blood products containing antibody (e.g., human anti-Rho [D] immune globulin) does not generally interfere with an immune response and is not a contraindication to postpartum vaccination. However, in this situation, serologic testing should be done 6-8 weeks after vaccination to assure that seroconversion has occurred.

Rubella vaccine should not be given to pregnant women or to those likely to become pregnant within 3 months after receiving the vaccine. Through 1983, CDC monitored prospective-ly 214 susceptible pregnant women who had received rubella vaccine within 3 months before or after conception and carried their pregnancies to term (94 received Cendehill or HPV-77, 119 received RA 27/3, and one received an unknown strain of vaccine). None of the infants had malformations compatible with CRS. The ACIP believes that the risk of vaccine-associated malformation is so small as to be negligible. Although a final decision must rest with the individual patient and her physician, the ACIP believes that rubella vaccination during pregnancy should not ordinarily be a reason to recommend interruption of pregnancy.

Because of the theoretical risk to the fetus, reasonable precautions should be taken before women of childbearing age are vaccinated. These precautions include 1) asking women if they are pregnant, 2) excluding those who say they are, and 3) explaining the theoretical risks of the vaccine to the others and counseling them not to become pregnant for 3 months after vaccination. If a pregnant woman is vaccinated or if a woman becomes pregnant within 3 months after vaccination, she should be counseled on the theoretical risks to the fetus. Instances of vaccination of *known* susceptible women who are pregnant or become pregnant within 3 months should be reported through state health departments to the Division of Immunization, CDC.

In general, rubella vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

Rubella vaccine is prepared in human diploid cell cultures and has not been reported to be associated with allergic reactions. The vaccine does contain trace amounts of neomycin to which patients may be allergic. Persons with a history of any sign or symptom of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) following receipt of neomycin should not receive rubella vaccine. Persons with reactions to neomycin that are not anaphylactic are not at increased risk and can be vaccinated. Rubella vaccine does not contain penicillin.

### ***Smallpox***

In May 1980, the World Health Organization (WHO) declared the world free of smallpox. A smallpox vaccination certificate is not required by any country as a condition of entry for international travelers. In May 1983, the distribution of smallpox vaccine for civilian use in the United States was discontinued.

#### ● **Vaccine indications**

There is no evidence that smallpox vaccination has therapeutic value in the treatment of recurrent herpes simplex infection, warts, or any other disease. Smallpox vaccine should never be used therapeutically for these or any other conditions.

Except for persons working with orthopox viruses or involved in producing and testing smallpox vaccine, there are *no* indications for the use of smallpox vaccine in civilian populations. When indicated, smallpox vaccination should be given at least every 3 years. For advice on vaccine administration and contraindications, contact the International Health Program Office, CDC, Atlanta, Georgia 30333.

### ***Yellow Fever***

Cases of yellow fever<sup>2</sup> are reported only from Africa and South America. Two forms of yellow fever—urban and jungle—are distinguishable epidemiologically. Clinically and etiologically they are identical.

Urban yellow fever is an epidemic viral disease transmitted from infected to susceptible persons by the *Aedes aegypti* mosquito. In areas where the *A. aegypti* mosquito has been eliminated or suppressed, urban yellow fever has disappeared. In West Africa, *A. aegypti*-transmitted epidemics involving town and village populations continue to occur at frequent intervals.

Jungle yellow fever is an enzootic viral disease transmitted among nonhuman hosts by a variety of mosquito vectors. It is currently observed only in forested areas of South America and forest-savannah zones of tropical Africa, but occasionally extends into Central America and the Caribbean. In tropical America 200-400 cases are recognized annually, mainly among persons with occupational exposure to the vector in forested areas; the disease is, however, believed to be greatly underreported. In Africa, epidemics that are spread by forest mosquito vectors affect tens of thousands of persons every few years, but few cases are officially reported. The jungle yellow fever cycle may be active but unrecognized in forested areas of countries within the zone with endemic yellow fever (Figure 1).

● **Yellow fever vaccine**

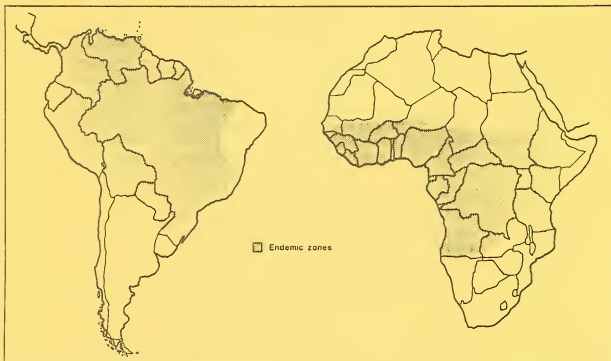
The yellow fever vaccine available in the United States is an attenuated, live-virus vaccine prepared from the 17D strain of virus grown in chick embryo. Immunity is induced by a single SC injection of 0.5 ml of reconstituted vaccine and persists for more than 10 years.

Yellow fever vaccines must be approved by WHO and administered at an approved Yellow Fever Vaccination Center. Centers can be identified by contacting state and local health departments. Vaccinees should have an International Certificate of Vaccination filled out, dated, signed, and validated with the stamp of the center where the vaccine is given. Vaccinee must be received 6 days to 10 years before travel in order for the certificate to be valid.

● **Vaccine indications**

Vaccination is recommended for persons traveling or living in areas where yellow fever infection occurs—currently parts of Africa and South America. Information on known or probably infected areas are published annually in *Health Information for International Travel*. Coun-

FIGURE 1. Yellow fever endemic zones



tries currently reporting yellow fever are noted biweekly in *Summary of Health Information for International Travel*. All state health departments and many county and city health departments receive these publications. It should be emphasized that the actual areas of yellow fever activity far exceed the zones officially reported to be infected. Vaccination is also recommended for laboratory personnel who might be exposed to virulent yellow fever virus.

Booster doses are needed at 10-year intervals.

Some countries, especially in Africa, require evidence of vaccination from all entering travelers. Other countries may waive the requirements for travelers coming from noninfected areas and staying less than 2 weeks. Some countries require a traveler, even if only in transit, to have a valid certificate if the traveler has visited any country thought to harbor yellow fever virus. Requirements of individual countries may change, and the most current information is published biweekly in *Summary of Health Information for International Travel* and summarized annually in *Health Information for International Travel*.

● **Vaccine side effects and adverse reactions**

Reactions to 17D yellow fever vaccine are generally mild. From 2% to 5% of vaccinees have mild headache, myalgia, low-grade fever, or other minor symptoms 5-10 days after vaccination. Fewer than 0.2% curtail regular activities. Immediate hypersensitivity reactions, characterized by rash, urticaria, and/or asthma, are extremely uncommon and occur principally in persons with a history of egg allergy. Although more than 34 million doses of vaccines have been distributed, only two cases of encephalitis temporally associated with vaccinations have been reported in the United States; in one fatal case, 17D virus was isolated from the brain.

● **Vaccine precautions and contraindications**

Yellow fever vaccine should not be given to persons who are immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or are immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

Although specific information is not available on adverse effects of yellow fever vaccine on the developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women and to advise that they postpone travel to areas where yellow fever occurs until after delivery. Pregnant women who must travel to areas where the risk of yellow fever is high should be vaccinated. It is believed that under these circumstances, the risk of yellow fever infection far outweighs the small theoretical risk to mother and fetus from vaccination. However, if international travel regulations constitute the only reason to vaccinate a pregnant woman or a patient hypersensitive to eggs, efforts should be made to obtain a letter of waiver from a physician clearly stating the contraindication to vaccination. Ideally, this letter should be written on letterhead stationery and bear the stamp used by health departments and official immunization centers to validate the International Certificates of Vaccination. Such a letter of waiver has been acceptable to some governments. Under these conditions, it is also useful for the traveler to obtain specific, authoritative advice from the country or countries he or she plans to visit. Their embassies or consulates may be contacted, and a letter substantiating the waiver of requirements obtained.

Since live yellow fever vaccine is produced in chick embryos, persons with a history of any signs or symptoms of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) after eating eggs should not receive yellow fever vaccine. If vaccination of an individual with a questionable history of egg hypersensitivity is considered essential because of a high risk of exposure, an intradermal (ID) test dose may be administered under close medical supervision. Specific directions for skin testing are found in the package insert.

Some data have indicated that persons given yellow fever and cholera vaccines simultaneously or 1-3 weeks apart had lower-than-normal antibody responses to both vaccines. Unless there are time constraints, cholera and yellow fever vaccines should be administered at a minimal interval of 3 weeks. If the vaccines cannot be administered at least 3 weeks apart, then they should preferably be given simultaneously.

Yellow fever vaccine and commercially available IG may be given simultaneously.

## Both Live-Virus and Inactivated-Virus Vaccines

### *Polio myelitis*

The risk of poliomyelitis is very small in the United States; however, epidemics could occur if the high immunity level of the general population is not maintained by immunizing children routinely or if wild poliovirus is introduced into susceptible populations in communities with low immunization levels. In the United States inapparent infection with wild poliovirus strains no longer contributes significantly to establishing or maintaining immunity. Most adults are already immune.

- **Poliovirus vaccines**

Two types of poliovirus vaccines are currently licensed in the United States: OPV and IPV. A primary vaccination series with either vaccine produces immunity to all three types of poliovirus in more than 95% of recipients. The primary series of OPV consists of three doses: two doses given 6-8 weeks apart and a third dose given at least 6 weeks and customarily 6-12 months after the second. The primary series for IPV consists of four doses: three doses each given 4-8 weeks apart and a fourth dose given 6-12 months after the third. In general, it is not necessary to give a primary vaccine series to adults living in the United States who have not had a primary series as children. However, for adults who have not had a primary series and who are at greater risk than the general population of exposure to wild polioviruses because of foreign travel or health occupation, IPV is preferred since the risk of OPV-associated paralysis is slightly higher in adults than in children.

Poliovirus vaccine is not routinely recommended for persons older than high school age (18-19 years old).

- **Vaccine indications**

Travelers to areas where wild poliovirus is epidemic or endemic should have completed a primary series of poliovirus vaccine. For previously unimmunized persons, IPV is indicated. However, if less than 4 weeks are available before protection is needed, a single dose of OPV is recommended. Travelers who have previously received less than a full primary course of OPV or IPV should be given the remaining required doses of either vaccine, regardless of the interval since the last dose and the type of vaccine previously received. Travelers to developing countries who have previously completed a primary series of OPV should receive a single dose of OPV. Additional booster doses of OPV are probably not necessary. Those who have previously received a primary series of IPV should receive a dose of either OPV or IPV. If IPV is used exclusively, an additional dose may be given every 5 years if exposure continues or recurs, although the need for these boosters has not been established.

Health-care personnel in close contact with patients who may be excreting wild polioviruses, and laboratory personnel handling specimens that may contain wild polioviruses, should have completed a primary series of poliovirus vaccine. IPV is indicated because of the slightly increased risk to adults of vaccine-associated paralysis after OPV administration; also, virus may be shed after receipt of OPV vaccine and inadvertently expose susceptible immunocompromised contacts to live vaccine virus.

- **Vaccine adverse reactions**

*Inactivated poliovirus vaccine.* No serious side effects of currently available IPV have been documented. Since IPV contains trace amounts of streptomycin and neomycin, hypersensitivity reactions are possible in individuals sensitive to these antibiotics. Persons with signs and symptoms of an anaphylactic reaction (i.e., hives, swelling of mouth and throat, difficulty in breathing, hypotension, or shock) following receipt of streptomycin or neomycin should not receive IPV. Persons with reactions that are not anaphylactic are not at increased risk and can be vaccinated.

*Oral poliovirus vaccine.* In rare instances, administration of OPV has been associated with paralysis in healthy recipients and their contacts. Although the risk of vaccine-associated paralytic poliomyelitis is extremely small for immunologically normal vaccinees (approximately one case per 9 million doses distributed) and their susceptible, immunologically normal household contacts (approximately one case per 7 million doses distributed), vaccinees should be informed of this risk.

- **Vaccine precautions and contraindications**

*Inactivated poliovirus vaccine.* There is no convincing evidence of adverse effects of IPV for the pregnant woman or developing fetus; regardless, it is prudent on theoretical grounds to avoid vaccinating pregnant women. However, if immediate protection against poliomyelitis is needed, OPV, not IPV, is recommended.

*Oral poliovirus vaccine.* Unlike other live-virus vaccines, which are administered parenterally, OPV is administered orally. IG and other antibody-containing blood products do not appear to interfere with the immune response to OPV.

OPV should not be given to persons who are or may be immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.) If immunization against poliomyelitis is indicated in such persons, IPV should be used, and some protection may result.

OPV should not be used for immunizing household contacts of patients immunocompromised as a result of immune deficiency disease, leukemia, lymphoma, or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. If protection is indicated, IPV should be used for immunizing household contacts of such patients. OPV should not be given to anyone in a family with a known family history of immunodeficiency until the immune status of all family members is documented.

When children in the household are given OPV, adults who are not adequately immunized against poliomyelitis are at a very small risk of contracting OPV-associated paralytic poliomyelitis. Because of the overriding importance of ensuring prompt and complete immunization of the child and the extreme rarity of OPV-associated disease in contacts of vaccinees, the ACIP recommends the administration of OPV to a child regardless of the poliovirus-vaccine status of adult household contacts. This is the usual practice in the United States. The responsible adult should be informed of the small risk involved and of precautions to be taken, such as hand washing after changing a diaper. An acceptable alternative, if there is strong assurance that ultimate, full immunization of the child will not be jeopardized or unduly delayed, is to immunize adults with IPV or OPV, as appropriate to their immunity status, before giving OPV to the child.

## **Inactivated-Virus Vaccines**

### ***Hepatitis B Virus Infection***

The estimated lifetime risk of acquiring HBV infection in the United States is approximately 5% for the population as a whole but may approach 100% for the highest risk groups. Annually, an estimated 100,000 symptomatic cases of hepatitis B disease occur in the United States, leading to approximately 10,000 hospitalizations and 190 fulminant cases. Three-fourths of persons with fulminant disease die.

In 1982, 88% of hepatitis B cases for which patient age was known occurred in persons 20 years of age or older. Between 6% and 10% of adults with HBV infection become carriers. The United States currently has 400,000-800,000 carriers. Chronic active hepatitis occurs in 25% of carriers. Each year in the United States, approximately 4,000 persons die of HBV-related cirrhosis, and 800, of HBV-related liver cancer.

#### ● **Hepatitis B vaccine**

A series of three 1-ml IM doses of HB vaccine, each containing 20  $\mu$ g/ml of HBsAg protein, provides protective antibody in over 90% of healthy adult recipients and is 80%-95% effective in preventing infection for at least 2 years. The first two doses should be given 1 month apart, and the third dose, 5 months after the second. The duration of vaccine-induced protection and the need for booster doses are not yet known. For susceptible hemodialysis patients, three 2-ml doses given at the above intervals are recommended. Because the prevalence of HBV varies widely among various population groups, serologic screening to detect susceptible individuals before vaccination may or may not be cost effective. Cost effectiveness depends on the known or perceived risk of infection, the cost of screening, and the cost of HB vaccine.

#### ● **Vaccine indications**

Immunization is recommended for adults at increased risk of occupational, social, family, environmental, or illness-related exposure to HBV. These include homosexual males, users of illicit injectable drugs, household and sexual contacts of HBV carriers, workers in health-related occupations requiring frequent exposure to blood, residents and staff of institutions for the mentally retarded, hemodialysis patients, recipients of factor VIII or IX concentrates, and morticians and their assistants. Inmates in some long-term correctional facilities may also be candidates for vaccination.

Vaccination should also be considered for persons who plan to reside for more than 6 months in areas with high levels of endemic HBV and who will have close contact with the local population and for travelers intending a short stay who are likely to have contact with blood from or sexual contact with residents of areas with high levels of endemic disease (particularly areas of eastern Asia and Sub-Saharan Africa). Such persons should allow 6 months before travel in order to complete the HB vaccine primary series.

HB vaccine is intended primarily for preexposure prophylaxis. However, it has recently been recommended for postexposure use in certain situations, particularly for persons who belong to a high-risk group for whom preexposure administration of vaccine is recommended (9). HB vaccine in combination with HBIG provides sustained protective levels of antibody and obviates the need for a second dose of HBIG in such exposures. Therefore, a normal series of HB vaccine, combined with a single dose (0.06 ml/kg or 5 ml for adults) of HBIG given at a different site, is recommended for postexposure prophylaxis of health workers following accidental percutaneous or mucous-membrane exposure to blood containing HBsAg, and of susceptible homosexual men following sexual exposure to an HBsAg-positive man. HBIG alone (in the same dose) is recommended for postexposure prophylaxis of persons with heterosexual exposures.



- **Vaccine side effects and adverse reactions**

In vaccine trials, soreness at the site of injection was the only side effect that occurred more frequently for vaccinees than for controls. Since its licensure in 1981 through August 1983, HB vaccine is estimated to have been administered to over 350,000 individuals in the United States. As of May 1984, adverse events following immunization had been reported for 890 vaccinees. The reported adverse events represent temporal associations with vaccination and are not necessarily caused by the vaccine. Forty-eight persons had serious events such as transverse myelitis, grand mal seizures, aseptic meningitis, erythema multiforme, or Guillain-Barré syndrome (GBS).

- **Vaccine precautions and contraindications**

Pregnancy should not be considered a contraindication to vaccinating women who are otherwise candidates for receiving HB vaccine. While data are not available on the safety of the vaccine for the developing fetus, HB vaccine contains only noninfectious HBsAg particles and should pose no risk to the fetus. In contrast, HBV infection in a pregnant woman may result in a severe disease for the mother and chronic infection for the newborn.

Since HB vaccine is made from human plasma, the possibility that it may contain an etiologic agent of acquired immunodeficiency syndrome (AIDS) has been raised. The purification and inactivation process used in preparing HB vaccine inactivates representatives of all known groups of viruses. There are no microbiologic, epidemiologic, or empiric data to suggest that the HB vaccine carries any etiologic risk for AIDS.

### ***Influenza***

Influenza viruses have continually demonstrated the ability to cause major epidemics of respiratory disease. High attack rates of acute illness and the frequent occurrence of lower-respiratory-tract complications usually result in dramatic rises in visits to physicians' offices and hospital emergency rooms. Furthermore, influenza frequently infects individuals who, because of their age or underlying health status, are poorly able to cope with the disease and often require medical attention, including hospitalization. Such persons are considered to be medically at "high risk" in epidemics. In one recent study, for example, rates of hospitalization for adults with "high-risk" medical conditions increased during major epidemics by about two- to fivefold in different age groups, reaching a maximum rate of about 800 per 100,000 population.

Influenza epidemics cause excess mortality, which is attributable not only to influenza pneumonia, but also to cardiopulmonary disease. Fifteen times in the years 1957-1982, epidemics have been associated with 10,000 or more excess deaths; in 1983, excess mortality again exceeded the epidemic threshold.

The greatest impact of influenza is normally seen when new strains appear against which most of the population lacks immunity. In these circumstances (e.g., 1957 and 1968), pandemics occur. During pandemics, a quarter or more of the United States population have been affected over a period of 2-3 months.

Because the proportion of elderly persons in the United States is increasing, and because age and its associated chronic diseases are risk factors for severe influenza illness, the toll of influenza may also increase unless control measures are used more vigorously than in the past.

- **Influenza vaccine**

Influenza A viruses are classified into subtypes on the basis of two antigens: hemagglutinin (H) and neuraminidase (N). Three subtypes of hemagglutinin (H1, H2, H3) and two subtypes of neuraminidases (N1, N2) are recognized among influenza A viruses that have caused widespread human disease. Immunity to these antigens, especially hemagglutinin, reduces the

likelihood of infection and the severity of disease if a person does become infected. However, there may be sufficient antigenic variation (antigenic drift) within the same subtype over time, so that infection or vaccination with one strain may not induce immunity to distantly related strains of the same subtype. Although influenza B viruses have shown much more antigenic stability than influenza A viruses, antigenic variation does occur. As a consequence, the antigenic characteristics of current strains provide the basis for selecting virus strains to be included in the vaccine for a given year.

Potency of present vaccines is such that nearly all vaccinated young adults develop hemagglutination-inhibition antibody titers that are likely to protect them against infection by strains like those in the vaccine, and often by related variants that emerge. The elderly, the very young, and patients with certain chronic diseases may develop lower postvaccination antibody titers than do young adults. Under these circumstances, influenza vaccine may be more effective in preventing lower-respiratory-tract involvement, or other complications of influenza, than in preventing upper-respiratory-tract involvement. Influenza vaccine will not prevent primary illnesses caused by other respiratory pathogens.

● **Vaccine indications**

Use of inactivated influenza vaccine is the single most important measure in the prevention and/or attenuation of influenza infection. Since 1963, annual vaccination against influenza has been recommended for individuals at high risk of lower-respiratory-tract complications and death following influenza infection (i.e., the elderly and persons with chronic disorders of the cardiovascular, pulmonary, and/or renal systems; metabolic diseases; severe anemia; and/or compromised immune function). These groups have been identified primarily by review of death certificate data, supported by hospital-based or population-based studies. Within each broadly defined "high-risk" category, however, some persons are more likely than others to suffer severe complications from influenza infection.

Among nursing-home residents, chronic diseases and other debilitating conditions are common, and spread of influenza can often be explosive, with attack rates as high as 60% and case-fatality ratios up to 30% or higher. In addition, recent retrospective studies of noninstitutionalized patients suggest that chronic underlying diseases, particularly those that affect the cardiovascular and pulmonary systems, may contribute more to the severity of illness than does age alone.

Medical personnel may transmit influenza infections to their high-risk patients while they are themselves incubating an infection, undergoing a subclinical infection, or working while they have mild symptoms. Nosocomial outbreaks of influenza are reported. The potential for introducing influenza to a high-risk group such as patients with severely compromised cardiopulmonary or immune systems or infants in neonatal intensive care units should be reduced by targeted vaccination programs of medical personnel.

Based on these observations, the previous, broadly defined "high-risk" adult groups have been further assigned priority for receiving vaccine in order that special efforts can be directed at providing vaccine to those who may derive the greatest benefit.

1. Adults at high risk of severe influenza illness who most warrant active, targeted vaccination efforts:
  - (a) Adults with chronic disorders of the cardiovascular or pulmonary systems that are severe enough to require regular medical follow-up or to have caused hospitalization during the preceding year.
  - (b) Residents of nursing homes and other chronic-care facilities (e.g., institutions housing patients of any age with chronic medical conditions). Achievement of high vaccination rates (e.g., 80%) may induce herd immunity in such populations and thereby

lower the frequency of outbreaks, as well as reducing the frequency of severe illness when outbreaks do occur.

2. Physicians, nurses, and other personnel who have extensive contact with high-risk patients (e.g., primary-care and certain specialty clinicians and staff of intensive-care units). These persons should receive influenza vaccination annually to reduce the possibility for nosocomial spread of influenza to high-risk patients.
3. Other adults who are at moderately increased risk of serious illness compared with the general population. Special programs to make vaccine readily available to these groups should also be given high priority:
  - (a) Healthy individuals over 65 years of age.
  - (b) Adults with a chronic metabolic disease (including diabetes mellitus), renal dysfunction (including those in chronic dialysis), anemia, immunosuppression, or asthma that is severe enough to require regular medical follow-up or to have caused hospitalization during the preceding year.

In addition, influenza vaccine may be offered to persons who provide essential community service or to any adult who wishes to reduce the likelihood of an influenza infection.

Effective programs for giving influenza vaccine are needed in nursing homes and other chronic-care facilities, in physicians' offices, and in hospital settings. Residents of nursing homes and chronic-care facilities should receive routine annual vaccination. Other adult high-priority groups should receive influenza vaccine at the time of regular medical follow-ups in the fall, or should be notified to come in specifically to receive the vaccine. Patients with high-risk conditions who are hospitalized during the fall should be considered for influenza vaccine before discharge from the hospital.

There is considerable overlap in the target groups for influenza vaccination and those for pneumococcal polysaccharide vaccine. Pneumococcal polysaccharide vaccine and influenza vaccine can be given at the same time at different sites without an increase in side effects; however, it should be emphasized that whereas influenza vaccine is given annually, pneumococcal polysaccharide vaccine should be given only once to adults. Detailed immunization records should be provided to each patient to help ensure that additional doses of pneumococcal polysaccharide vaccine are not given.

Amantadine hydrochloride, an antiviral drug, can prevent influenza A or be used therapeutically to reduce symptoms of influenza A infections. It is *not* a substitute for vaccine. Specific circumstances in which amantadine prophylaxis is recommended are described in the ACIP recommendations on prevention and control of influenza.

#### ● Vaccine side effects and adverse reactions

Vaccines used in recent years have generally been associated with only a few reactions. Fewer than one-third of vaccinees have been reported to develop local redness or induration for 1 or 2 days at the site of injection.

Systemic reactions have been of two types. First, malaise, myalgia, and other systemic symptoms of toxicity, although infrequent, most often affect those who have had no experience with the influenza virus antigens contained in the vaccine. These reactions, which begin 6-12 hours after vaccination and persist for 1-2 days, are usually attributed to the influenza antigens (even though the virus is inactivated) and constitute most of the systemic side effects of influenza vaccination.

Second, immediate, presumably allergic, responses such as flare and wheal or various respiratory-tract symptoms of hypersensitivity occur extremely rarely after influenza vaccination. These symptoms probably result from sensitivity to some vaccine component—most likely residual egg protein. Although current influenza vaccines contain only a small quantity of egg protein, on rare occasions vaccine can induce hypersensitivity reactions. Unlike the

1976 swine influenza vaccine, vaccines used subsequently have not been associated with an increased frequency of GBS.

- **Vaccine precautions and contraindications**

Pregnancy has not been demonstrated to be a risk factor for severe influenza infection except in the largest pandemics of 1918-1919 and 1957-1958. Influenza vaccine is considered to be generally safe for pregnant women. Nonetheless, when vaccine is to be given during pregnancy, waiting until the second or third trimester is a reasonable precaution to minimize any concern over theoretical teratogenicity.

Persons with a history of any signs or symptoms of an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) after eating eggs should not be given inactivated influenza vaccine.

Persons with acute febrile illnesses normally should not be vaccinated until their temporary symptoms have abated.

### ***Rabies***

Although rabies rarely affects humans in the United States, thousands of persons receive rabies vaccine every year, principally for postexposure prophylaxis. The likelihood of human exposure to rabies from domestic animals has decreased greatly in recent years. In every year since 1976, more than 85% of all reported cases of animal rabies have been among wild animals, the most important source of possible infection for humans in the United States. However, for persons traveling overseas to developing countries with endemic rabies, the dog remains the animal most likely to transmit rabies.

- **Rabies vaccine**

Both whole-virion and subvirion human diploid cell rabies vaccines (HDCV) are available. For preexposure rabies prophylaxis a three-dose series of HDCV of either type given as 1-ml doses IM on days 0, 7, and 28 provides adequate antibody levels in virtually all recipients (10). The CDC currently accepts a titer of 5 by the rapid fluorescent-focus inhibition test as adequate.

The whole-virion HDCV produced by the Merieux Institute has been used for preexposure immunization in a regimen of three 0.1-ml doses given intradermally (ID) in the lateral aspect of the upper arm in the deltoid area, one dose on each of days 0, 7, and 28. Experience gained with over 2,000 persons vaccinated in the United States by the ID route has shown that antibody is produced in all recipients, although the mean response is somewhat lower and may be of shorter duration than with comparable IM immunization. Except for persons suspected of being immunosuppressed, postvaccination serology is not necessary following IM or ID immunization in the United States. Antibody response in some groups vaccinated ID outside the United States has been found to be inadequate for reasons not yet determined (11). Preliminary data suggest that concurrent administration of malaria chemoprophylaxis may be a factor in the lowered immunologic response of persons vaccinated overseas. It should be noted that Merieux Institute, the manufacturer, has not yet met the packaging and labeling requirements necessary to obtain approval by the FDA for the ID route of administration. The 1-ml vial presently available is intended for IM use and contains no preservatives. To minimize the risk of contamination and loss of vaccine potency, the reconstituted vaccine must be used immediately. Data on ID immunization are not available for Wyeth Laboratories vaccine.

Proper postexposure rabies prophylaxis is determined by whether or not the person has had previous preexposure or postexposure prophylaxis. 1) Persons who (a) have previously received postexposure prophylaxis with HDCV, (b) have received a three-dose IM preexposure regimen of HDCV, (c) have received a three-dose ID preexposure regimen of HDCV in the

United States, or (d) have a previously documented adequate rabies titer should receive two 1-ml IM doses of HDCV—one dose on each of days 0 and 3. HRIG is not recommended in these circumstances. 2) Persons not meeting the above criteria should be treated with a single, 20-international units (IU)/kg dose of HRIG and five 1-ml doses IM of HDCV—one on each of days 0, 3, 7, 14, and 28. HRIG should be administered at the beginning of HDCV post-exposure prophylaxis but can be given up to the eighth day after the first dose of HDCV was given. The HRIG dose should be divided; up to half should be infiltrated into the area of the wound, if possible, and the rest administered IM, but not in the same site as HDCV. Only IM administration of HDCV is indicated for postexposure prophylaxis.

● **Vaccine indications**

Preexposure immunization should be considered for high-risk groups: animal handlers, certain laboratory workers and field personnel, and persons planning to be in countries or areas of countries for more than 1 month where rabies is a constant threat. Persons whose vocations or avocations bring them into contact with potentially rabid animals should also be considered for preexposure immunization. Persons with continuing risk of exposure should receive a booster dose every 2 years or have their serum tested for rabies antibody every 2 years and, if the titer is inadequate, be given a booster dose. If there is substantial risk of exposure to rabies, preexposure rabies prophylaxis may be indicated during pregnancy.

The decision to provide specific postexposure antirabies treatment should include the following considerations:

1. Type of exposure—rabies is transmitted primarily by the bite of infected animals. It may also be transmitted by introducing the virus into open cuts or wounds in skin or via mucous membranes by saliva or other potentially infectious material from a rabid animal and, rarely, by aerosol exposure.
2. Species of biting animal—carnivorous wild animals (especially skunks, raccoons, and foxes) and bats are most commonly infected with rabies in the United States. Elsewhere in the world, dogs, cats, carnivorous wildlife, and bats are the major vectors. The likelihood that domestic cats or dogs in the United States will be infected varies from region to region. Rodents are rarely infected. Consultations with the state or local health department may be helpful.
3. Circumstances of biting incident—an unprovoked attack is more indicative of a rabid animal than a provoked attack.

● **Vaccine side effects and adverse reactions**

Following postexposure prophylaxis, local reactions, such as pain, erythema, and swelling or itching at the injection site, are very common, and mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness, are reported by about 20% of recipients. Systemic allergic reactions ranging from hives to anaphylaxis occur in an estimated 11 per 10,000 vaccinees. Mild immune-complex-like hypersensitivity reactions consisting of hives, itching, and angio-edema have occurred 2-21 days after booster doses of HDCV and are the most frequently reported allergic reactions (12). Four cases of transient neuromuscular illness have been temporally associated with HDCV administration: two following administration of whole-virion vaccine and two following administration of subvirion vaccine (13). No permanent sequelae or deaths have been associated with administration of HDCV.

● **Vaccine precautions and contraindications**

Corticosteroids and other immunosuppressive agents can interfere with the development of active immunity and should not be administered during preexposure therapy. When rabies postexposure prophylaxis is administered to persons known or suspected of being immunosuppressed, or to those who are receiving steroids or immunosuppressive therapy, it is especially important that serum be tested to ensure an adequate rabies antibody response.

If a person experiences an anaphylactic reaction (i.e., hives, swelling of the mouth and throat, difficulty in breathing, hypotension, or shock) after receiving HDCV, no further preexposure doses of HDCV should be given. By contrast, if a person needing postexposure therapy has had a previous anaphylactic reaction to HDCV or has such a reaction during the postexposure course, HDCV therapy should continue; however, the person should receive the required doses in an appropriate medical setting.

## Inactivated-Bacteria Vaccines

### *Cholera*

Cholera continues to be a health risk in Africa and Asia. Countries currently reporting cholera are listed in the biweekly publication *Summary of Health Information for International Travel*. All state health departments and many county and city health departments receive this publication. Persons who follow the usual tourist itinerary and who use tourist accommodations in countries affected by cholera are at virtually no risk of infection. The traveler's best protection against cholera is avoiding food and water that might be contaminated.

- **Cholera vaccine**

The vaccine may be administered as a 0.5-ml dose SC or IM or as a 0.2-ml dose ID. Although a single dose of vaccine is sufficient for entry into most countries, some countries may require evidence of a complete primary series of two doses given 1 week to 1 month or more apart, or a booster dose within 6 months before arrival.

The currently available cholera vaccine has been shown in field trials to be only about 50% effective in preventing clinical illness for a period of 3-6 months. The vaccine does not prevent transmission of infection. The risk of cholera to most U.S. travelers is so low that it is doubtful that vaccination is of benefit. WHO no longer recommends cholera vaccination for travel to or from cholera-infected areas. However, some countries affected or threatened by cholera require evidence of cholera vaccination as a condition of entry. Current information on cholera-vaccination requirements of individual countries is published annually in *Health Information for International Travel*. All state health departments and many county and city health departments receive this publication. Travelers to countries with cholera-vaccination requirements should have an International Certificate of Vaccination filled in, dated, signed, and validated showing receipt of the vaccine 6 days to 6 months before entry into the country. Most city, county, and state health departments can validate certificates. Failure to secure validation may cause travelers to be revaccinated or quarantined.

- **Vaccine indications**

Cholera vaccine is indicated only for travelers to countries requiring evidence of cholera vaccination for entry. Boosters may be given every 6 months if required by a country.

- **Vaccine side effects and adverse reactions**

Vaccination often results in 1-2 days of pain, erythema, and induration at the site of injection. The local reaction may be accompanied by fever, malaise, and headache. Serious reactions, including neurologic reactions, following cholera vaccination are extremely rare.

- **Vaccine precautions and contraindications**

No specific information is available on the safety of cholera vaccine during pregnancy. Because cholera disease during pregnancy is a serious illness, whether to use cholera vaccine should be determined in individual circumstances based on the actual risk of disease and the probable benefits of the vaccine.

The only contraindication to cholera vaccine is a history of a severe reaction following a previous dose. Most governments will permit an unvaccinated traveler to enter the country if

he or she carries a physician's statement of medical contraindication. However, some countries may quarantine such unvaccinated persons or place them under surveillance if they come from areas with cholera.

Some data have indicated that persons given yellow fever and cholera vaccines simultaneously or 1-3 weeks apart had lower-than-normal antibody responses to both vaccines. Unless there are time constraints, cholera and yellow fever vaccines should be administered at a minimal interval of 3 weeks. If the vaccines cannot be administered at least 3 weeks apart, then they should preferably be given simultaneously.

### ***Meningococcal Disease***

Meningococcal disease is endemic throughout the world but may also occur in epidemics. Among U.S. civilians, meningococcal disease occurs primarily as single, isolated cases or, infrequently, in small, localized clusters. A third of all cases of meningococcal disease occur in patients 20 years old or older. Serogroup B strains cause the majority of U.S. cases, with serogroups C and W135 strains accounting for most of the remainder.

- **Meningococcal polysaccharide vaccine**

Two meningococcal polysaccharide vaccines, bivalent A-C and quadrivalent A, C, Y, and W135 vaccines, are available for use in the United States. Each is given as a single dose, and each induces specific serogroup immunity. The duration of immunity conferred by the vaccines is not known.

- **Vaccine indications**

Vaccine may be of benefit as an adjunct to antibiotic chemoprophylaxis for household and other close contacts of persons with meningococcal disease caused by serogroups A, C, Y, and W135 and for travelers to areas with epidemic meningococcal disease. The need for booster doses has not been established.

Routine vaccination of U.S. civilians with meningococcal polysaccharide vaccine is *not* recommended because of the lack of availability of a group B vaccine and the low risk of infection in the United States.

- **Vaccine side effects and adverse reactions**

Adverse reactions to meningococcal polysaccharide vaccines are infrequent and mild, consisting principally of localized erythema lasting 1-2 days.

- **Vaccine precautions and contraindications**

The safety of meningococcal polysaccharide vaccines for pregnant women has not been established. On theoretical grounds, it is prudent not to use them unless there is a substantial risk of infection.

### ***Plague***

Plague is a natural infection of rodents and their fleas. In the United States a few human cases occur yearly in humans exposed in the Western states to infected animals, primarily rodents, and their fleas. Other countries currently reporting plague infections are noted in the biweekly publication *Summary of Health Information for International Travel*. All state health departments and many county and city health departments receive this publication. A number of countries in Africa, Asia, and South America continue to report sporadic, epidemic, and epizootic infection. In most of these countries, the risk of exposure exists primarily in rural or semirural areas.

- **Plague vaccine**

A primary series of plague vaccine consists of three IM doses. The first dose, 1 ml, is followed in 4 weeks by a second dose of 0.2 ml. The third dose, also 0.2 ml, is administered 5

months after the second. The effectiveness of a primary series of plague vaccine has never been measured precisely. Field experience indicates that vaccination with plague vaccine reduces the incidence and severity of disease resulting from the bite of infected fleas. The degree of protection offered against primary pneumonic infection is unknown. Since plague vaccination may only ameliorate illness, prophylactic antibiotics may be indicated whenever a person, vaccinated or not, has a definite exposure.

- **Vaccine indications**

Vaccination is indicated for certain vocational groups. These include all laboratory and field personnel working with *Yersinia pestis* organisms that may be resistant to antimicrobials, persons engaged in aerosol experiments with *Y. pestis*, and field personnel engaged in operations in areas with enzootic or epidemic plague where preventing exposure to rodents and fleas is impossible. Plague vaccination should be considered for laboratory personnel regularly working with *Y. pestis* or plague-infected rodents and for persons whose vocation regularly exposes them to wild rodents or rabbits in areas with enzootic plague.

Vaccine may also be considered for travelers to areas known to have endemic plague in countries reporting plague, particularly if travel will not be limited to urban areas with tourist-hotel accommodations.

For persons with continuing exposure, three booster doses, each 0.1-0.2 ml, should be given at approximately 6-month intervals. Thereafter, booster doses at 1- to 2-year intervals should provide good protection.

- **Vaccine side effects and adverse reactions**

For about 10% of recipients, primary vaccination may result in general malaise, headache, fever, mild lymphadenopathy, and/or erythema and induration at the injection site. These reactions occur more commonly with repeated injections. Sterile abscesses occur rarely. Sensitivity reactions manifested by urticarial and asthmatic phenomena have occasionally been reported.

- **Vaccine precautions and contraindications**

Neither the safety nor efficacy of vaccination with plague vaccine during pregnancy has been determined; therefore, it should not be used unless there is a substantial risk of infection.

Plague vaccine should not be administered to anyone with a known hypersensitivity to any of its constituents (beef protein, soy, casein, and phenol). Patients who have had severe local or systemic reactions to plague vaccine should not be revaccinated.

### ***Pneumococcal Disease***

Precise data on the occurrence of serious pneumococcal disease in the United States are not available; however, the annual incidence rate of pneumococcal pneumonia is estimated to be 68 cases to 260 cases per 100,000 population, and of bacteremia, 7-25/100,000. The incidence of pneumococcal pneumonia, which causes a substantial number of deaths annually, increases in those over 40 years old, and shows a twofold increase in those over 60 years of age. Mortality from pneumococcal disease is highest among patients who have bacteremia or meningitis, patients with underlying medical conditions, and older persons.

Patients with certain underlying conditions are clearly at increased risk both of contracting pneumococcal infection and of experiencing more severe pneumococcal illness. These conditions include sickle cell anemia, multiple myeloma, cirrhosis, alcoholism, nephrotic syndrome, renal failure, splenic dysfunction, anatomic asplenia, and organ transplant. Persons suffering from diabetes mellitus, chronic pulmonary disease, cardiovascular disease, or conditions associated with immunosuppression may be at increased risk of contracting pneumococcal infection or of having more severe illness.



- **Pneumococcal polysaccharide vaccine**

The pneumococcal polysaccharide vaccine currently available contains purified capsular materials of the 23 types of *Streptococcus pneumoniae* responsible for 87% of recent bacteremic pneumococcal disease in the United States. Most healthy adults show a twofold rise in type-specific antibody 2-3 weeks after administration of a single dose of vaccine. The titer of antibody that is protective against each serotype has not been determined.

The duration of vaccine-induced immunity is unknown. Studies of persistence of vaccine-induced antibody show elevated titers 3-5 years after immunization. Booster doses are not recommended because of increased adverse reactions to subsequent doses.

Patients who have received the earlier pneumococcal polysaccharide vaccine containing capsular material from only 14 types of *S. pneumoniae* should not receive a dose of the 23-valent pneumococcal polysaccharide vaccine since the modest increase in coverage does not warrant the increased risk of adverse reactions.

- **Vaccine indications**

Newly available data regarding vaccine efficacy support the broader use of pneumococcal polysaccharide vaccine in the United States. Vaccination is particularly recommended for the following:

- 1) Adults with chronic illnesses, especially those with cardiovascular disease and chronic pulmonary disease, who sustain increased morbidity with respiratory infections.
- 2) Adults with chronic illnesses specifically associated with an increased risk of pneumococcal disease or its complications. These include splenic dysfunction or anatomic asplenia, Hodgkins' disease, multiple myeloma, cirrhosis, alcoholism, renal failure (including those on chronic dialysis), cerebrospinal-fluid leaks, and conditions associated with immunosuppression.
- 3) Older adults, especially those age 65 and over, who are healthy.

Programs for vaccine delivery in the recommended high-risk groups need to be developed further. Specifically, more effective programs are needed for giving vaccine in physicians' offices, in hospitals, and in nursing homes and other chronic-care facilities.

Since two-thirds of persons with serious pneumococcal disease have been hospitalized within 5 years before the pneumococcal illness (14), vaccine should be given to hospitalized patients in the high-risk groups before discharge, in order to prevent future admissions for pneumococcal disease. In addition, persons with chronic conditions who visit physicians frequently are probably at higher risk of pneumococcal infection than those who require infrequent visits. Office-based programs to identify and immunize patients requiring frequent medical care should help prevent pneumococcal illness. Furthermore, pneumococcal polysaccharide vaccine and influenza vaccine can be given at different sites at the same time without an increase in side effects (15).

Medicare has partially reimbursed the cost of pneumococcal polysaccharide vaccination since 1981. It has been determined that hospitals may be reimbursed for pneumococcal immunization of Medicare recipients independent of reimbursement based on systems of prospective payments.

- **Vaccine side effects and adverse reactions**

About half of the persons given pneumococcal polysaccharide vaccine experience mild side effects such as erythema and pain at the site of injection. Fever and myalgias have been reported by fewer than 1% of those given pneumococcal polysaccharide vaccine (16). Severe adverse effects such as anaphylactic reactions have rarely been reported—about five cases per million doses administered.

Arthus reactions and systemic reactions have been common among adults given second

doses (17). They are thought to result from localized antigen-antibody reactions involving antibody induced by previous vaccination. Therefore, second, or "booster," doses are not recommended.

- **Vaccine precautions and contraindications**

The safety of pneumococcal polysaccharide vaccine in pregnant women has not been evaluated. It should not be given to healthy pregnant women. Women at high risk of pneumococcal disease ideally should be vaccinated before pregnancy.

Because of a marked increase in adverse reactions with second injections of pneumococcal polysaccharide vaccine, second, or "booster," doses should not be given. However, when there is doubt or no information on whether a person in one of the high-risk groups has ever received pneumococcal polysaccharide vaccine, vaccine should be given. Complete records of vaccination can help to avoid repeat doses.

### *Typhoid*

The occurrence of typhoid fever remained constant in the period 1972-1982, with an average of 486 cases reported annually. During the years 1978-1982, 57% of cases for which the patient's age was known occurred in patients 20 years of age or older. Approximately 62% of typhoid cases reported in the United States during 1977-1979 were acquired by travelers to other countries, and an additional 27% occurred in contacts of typhoid carriers.

- **Typhoid vaccine**

A primary series of two 0.5-ml doses of typhoid vaccine given SC 4 weeks apart has been shown to protect 70%-90% of recipients.

- **Vaccine indications**

Immunization is indicated for travelers to areas where a recognized risk of exposure to typhoid exists. It should be emphasized that even after typhoid vaccination, food and water should be selected carefully in these areas. Typhoid vaccination is not recommended in the United States or in areas of natural disaster. Booster doses should be given at least every 3 years to persons with continued or repeated exposure; these may be given SC (0.5 ml) or ID (0.1 ml). The acetone-killed and -dried vaccine should not be given ID. This preparation is available only to the U.S. Armed Forces.

- **Vaccine side effects and adverse reactions**

Typhoid vaccination often results in 1-2 days of discomfort at the site of injection. The local reaction may be accompanied by fever, malaise, and headache.

- **Vaccine precautions and contraindications**

The only contraindication to typhoid vaccine is a history of a severe local or systemic reaction following a previous dose.

## **Live-Bacteria Vaccines**

### *Tuberculosis*

The number of tuberculosis cases in the United States has declined steadily since reporting began in the 19th century. Between 1972 and 1982, the annual incidence of tuberculosis declined from 15.8 cases per 100,000 population to 11.0/100,000, a decrease of 30%. In 1982, approximately 92% of 25,059 reported cases with patient ages known occurred in persons 20 years of age or older. Reported cases usually are typical postprimary pulmonary disease. The risk of infection is greatest for those who have repeated exposure to persons with unrecognized or untreated sputum-positive pulmonary tuberculosis. In the United States, efforts to control tuberculosis are directed toward early identification and treatment of cases,

preventive therapy with isoniazid for infected persons at high risk of developing disease, and prevention of transmission to others.

- **BCG vaccine**

Although BCG vaccine is widely used in many areas of the world, results of a recent large-scale field trial in India have raised questions about its efficacy (18). BCG vaccines currently available in the United States differ from the products used in the published field trials, and their efficacy has not been demonstrated directly. In the United States, vaccines for ID and for percutaneous administration are licensed. (For percutaneous administration, one drop of vaccine is placed on the skin and introduced through the skin by multiple punctures with a bifurcated or other needle.) Vaccination should be only by the route indicated on the package labeling.

- **Vaccine indications**

In the United States the only situations in which BCG might be considered are 1) for individuals in prolonged close contact with patients with active tuberculosis that is untreated, ineffectually treated, or resistant to treatment; 2) for health-worker groups, such as hospital staffs, with an annual new-infection rate of 1% or higher in spite of other tuberculosis control measures; and 3) for other groups in which an excessive rate of new infection can be demonstrated and the usual surveillance and treatment programs have failed or are not feasible.

- **Vaccine side effects and adverse reactions**

BCG has been associated with severe or prolonged ulceration at the vaccination site, regional adenitis, disseminated BCG infection, and osteitis. Severe ulceration and adenitis occur in approximately 1%-10% of vaccinees, and disseminated infections and osteitis are quite rare (1-10 per million doses).

- **Vaccine precautions and contraindications**

Although no harmful effects of BCG on the fetus have been observed, it is prudent to avoid vaccination during pregnancy unless there is immediate excessive risk of exposure to infective tuberculosis.

Since BCG is a live-bacteria vaccine, it should not be given to persons immunocompromised as a result of immune deficiency diseases, leukemia, lymphoma, or generalized malignancy or to persons immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. (See "Conditions That Compromise the Immune System," page 8S.)

## **Other Licensed Vaccines**

### ***Adenovirus and Adenovirus Vaccine***

Adenovirus types 4 and 7 have frequently been the cause of outbreaks of acute, febrile, respiratory-tract disease in young adults during military training. Live, oral adenovirus vaccines for types 4 and 7 are available for immunization of military populations. Use of the vaccines in other populations is not recommended.

### ***Anthrax and Anthrax Vaccine***

Anthrax is infrequently encountered. Anthrax vaccine is recommended only for individuals who come in contact with imported animal hides, furs, bonemeal, wool, animal hair (especially goat hair), and bristles in the workplace and for individuals undertaking investigational studies involving *Bacillus anthracis*.

Primary immunization consists of six SC 0.5-ml injections, the first three at 2-week intervals and the other three at 6-month intervals. Booster doses of 0.5-ml SC are recommended at 1-year intervals. The vaccine is only available from the Biologic Products Program, Michi-

gan Department of Public Health. Details on reactions and vaccine contraindications are found in the package insert.

### ***Pertussis and Pertussis Vaccine***

Pertussis disease in adults is generally milder than in children and is not known to result in death. Pertussis can be transmitted from adult patients to close contacts, especially unimmunized children. Such transmission may occur in the household and in hospitals, where chains of transmission have involved patients and staff.

In general, pertussis vaccine is not recommended for adults because both local and systemic reactions are thought to be more frequent and severe than in children under 7 years of age and because the disease itself is less severe in adults. In specific situations, such as documented transmission to and from personnel in a hospital, single-antigen pertussis vaccine in a 0.2-ml IM dose has been given as a part of control efforts. Single-antigen pertussis vaccine, adsorbed, is available only from the Biologic Products Program, Michigan Department of Public Health.

### **Immune Globulins**

IG and specific immune globulins, i.e., HBIG, TIG, HRIG, and varicella zoster immune globulin (VZIG), are indicated for use in order to prevent or modify certain diseases in specific circumstances.

#### ***Immune Globulin for intramuscular Use***

IG is given IM for preexposure prophylaxis against hepatitis A to travelers in areas where contact with potentially contaminated food and water is unavoidable. For travelers at risk for 2-3 months, a single IM dose of 0.02 ml/kg is recommended. For more prolonged travel 0.06 ml/kg should be given every 5 months. IG is also indicated for postexposure prophylaxis for close household and sexual contacts of persons with hepatitis A, staff and attendees of day-care centers and household contacts of diapered children in day-care centers in which hepatitis A transmission is occurring, selected staff and clients of custodial institutions in which an outbreak is occurring, and co-workers of food handlers with hepatitis A. For such contacts a single dose of 0.02 ml/kg of IG is recommended as soon as possible after exposure. IG should be given within 2 weeks after exposure.

IG can be used to prevent or modify measles disease in susceptible contacts of persons with measles, especially those for whom measles vaccine is contraindicated, if given within 6 days after exposure. The recommended dose is 0.25 ml/kg (maximum dose = 15 ml). IG should not be used to control measles outbreaks.

#### ***Immune Globulin for Intravenous Use***

IG modified for IV administration may be given to prevent acute infections in patients with defective antibody synthesis or as prophylaxis against hepatitis A for patients for whom the IM preparation is contraindicated because of thrombocytopenia or disorders that can cause IM hemorrhage. ONLY IG MODIFIED FOR INTRAVENOUS USE CAN BE GIVEN INTRAVENOUSLY. The IV dose is 100 mg/kg, given slowly. The IV preparation is supplied in 50-ml vials containing 2.5 g of IG.

#### ***Hepatitis B Immune Globulin***

HBIG, alone or in combination with HB vaccine, is used for postexposure prophylaxis of HBV infection. For percutaneous or mucous membrane exposure to blood known to be HBsAg

positive or from a bite by an HBV carrier, a single dose of HBIG (0.06 ml/kg or 5 ml for adults) should be given as soon as possible, and a series of three doses of HB vaccine begun within 1 week after exposure. Vaccine and HBIG may be given simultaneously, but in different sites. For those who choose not to take HB vaccine, a second identical dose of HBIG should be given 1 month later.

Following percutaneous exposure to blood from individuals at high risk of being HBsAg positive (such as persons with acute, unconfirmed viral hepatitis) or from patients at high risk of being infected with hepatitis B (such as male homosexuals, users of illicit IV drugs, and hemodialysis patients), IG should be given immediately to the exposed person as an IM dose of 0.06 ml/kg. Then serologic confirmation of the HBsAg status of the suspected high-risk patient should be obtained as soon as possible, and certainly within 7 days. If the suspected high-risk patient is HBsAg positive, the exposed person should immediately receive HBIG and hepatitis B vaccine according to the schedule above. The value of HBIG given beyond 7 days after exposure is unclear.

For homosexual exposure to HBsAg-positive males (known carriers or persons with acute cases), a single dose of HBIG should be given to susceptible contacts within 14 days after the last sexual exposure. Since HB vaccine is routinely recommended for male homosexuals, an HB vaccine series should be started within 7 days after HBIG administration.

For heterosexual exposures to persons with acute cases of hepatitis B, a single dose of HBIG (0.06 ml/kg or 5 ml for adults) should be given within 14 days of the last sexual contact. If the index case remains HBsAg positive at 3 months and exposure continues, the contact should be given a second dose of HBIG. If the index case becomes an HBV carrier (HBsAg positive for 6 months), the HB vaccine series should be given to the contact.

### ***Tetanus Immune Globulin***

TIG is indicated in tetanus prophylaxis as part of the management of wounds other than clean, minor wounds in persons 1) whose previous tetanus toxoid immunization status is unknown or uncertain, 2) who have received fewer than two previous tetanus toxoid doses, or 3) who have received only two previous tetanus toxoid doses and whose wound is more than 24 hours old. The currently recommended prophylactic dose for wounds of average severity is 250 units IM. Td should be given at the same time but at a separate site.

A summary of the indications for active and passive immunization in the management of wounds is provided in Table 5.

### ***Human Rabies Immune Globulin***

Postexposure prophylaxis for rabies should always include HRIG with one exception: persons who have been previously immunized with the recommended preexposure or postexposure regimens of HDCV or have been immunized with other types of rabies vaccines and have a history of documented adequate rabies antibody titer should not receive HRIG (Table 4). The recommended dose of HRIG is 20 IU/kg body weight. If anatomically feasible, up to one-half the dose of HRIG should be thoroughly infiltrated in the area around the wound, the rest should be administered IM.

### ***Varicella-Zoster Immune Globulin***

Most adults (85%-95%) with negative or unknown histories of varicella disease (chickenpox) are likely to be immune. (Susceptibility rates for adults raised in some tropical areas, particularly remote areas, may be somewhat higher.) Rates of complications and death for immunocompromised adults who contract varicella are likely to be substantially greater than for

normal adults. After careful, individual evaluation, an immunocompromised patient who is believed to be susceptible and who has had significant exposure to varicella should receive VZIG to prevent complications.

Significant exposure to a person with varicella includes household contact, close contact indoors of longer than 1 hour, sharing the same two- to four-bed hospital room, or prolonged, direct, face-to-face contact such as occurs with nurses or doctors who take care of the patient.

Chickenpox can be more severe in adults than in normal children. The decision to administer VZIG to a normal adult should be made on an individual basis. The objective of VZIG use for normal adults is to modify rather than prevent illness in hopes of inducing lifelong immunity. When deciding whether to administer VZIG, the clinician should consider the patient's health status, the type of exposure, and the likelihood of previous infection. It is likely that adults who were older siblings in large families or whose children have had varicella are immune. If, after careful evaluation, a normal adult with significant exposure to varicella is believed to be susceptible, VZIG may be administered. Pregnant women and potentially susceptible hospital personnel should be evaluated in the same way as other adults. Supplies of VZIG are limited, and indiscriminate administration of VZIG to normal adults would quickly exhaust supplies and prevent prophylaxis for known high-risk individuals. The cost of a five-vial adult dose is approximately \$375.

VZIG, available through some American Red Cross distribution centers (Appendix 5), is supplied in vials containing 125 units. Whereas 125 units/10 kg of body weight up to a maximum of 625 units generally is considered likely to prevent or modify varicella in normal adults, higher doses may be necessary for the immunocompromised adult. However, the appropriate dose for immunocompromised adults has not been determined. VZIG should be administered IM as directed by the manufacturer. While the duration of protection is unknown, it seems reasonable that protection should last for at least one half-life of the immune globulin, that is, approximately 3 weeks.

### ***Immune Globulin Side Effects and Adverse Reactions***

Serious adverse effects have been rare from immune globulins administered as recommended.

### ***Immune Globulin Precautions and Contraindications***

Immune globulins, if needed, are not contraindicated for pregnant women. Except for the IV preparation of IG, immune globulins are prepared for IM use and should *not* be given IV. The various preparations intended for IM use should not be given to patients with severe thrombocytopenia or other coagulation disorders that would ordinarily contraindicate IM injections unless the expected benefits outweigh the risks.

Parenterally administered live-virus vaccines (e.g., MMR or other combinations) should be given at least 14 days before or at least 6 weeks, and preferably 3 months, after the administration of immune globulins. If an immune globulin must be administered within 14 days after the administration of most live-virus vaccines, the vaccine should be administered again 3 months after the immune globulin is given. If the interval between vaccine receipt and immune globulin receipt is longer, the vaccine need not be readministered.

Preliminary data indicate that immune globulins do not interfere with the immune response to either OPV or yellow fever vaccine.

In July 1983, a WHO Consultative Group reviewed data on both normal and specific immune globulins prepared from plasma collected mainly in the United States, including dona-

tions from homosexuals. The data indicated that although about 19.5 million 2-ml to 10-ml doses of immune globulin had been prepared during the preceding 4 years, no transmission of hepatitis B or any other infectious agents and no cases of AIDS had been reported in persons observed for 1-4 years after receiving immune globulin. Therefore, the Consultative Group confirmed that, at present, there is no evidence of risk attached to the use of normal or specific immune globulins prepared by the universally accepted methods (19).

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**TABLE 1. Vaccines and toxoids recommended for adults in general, by age groups**

| Age group   | Vaccine or toxoid |                |                |                |           | Pneumococcal polysaccharide |
|-------------|-------------------|----------------|----------------|----------------|-----------|-----------------------------|
|             | Td*               | Measles        | Mumps          | Rubella        | Influenza |                             |
| 18-24 years | X                 | X              | X <sup>§</sup> | X              |           |                             |
| 25-64 years | X                 | X <sup>†</sup> | X <sup>§</sup> | X <sup>¶</sup> |           |                             |
| ≥65 years   | X                 |                |                |                | X         | X                           |

**NOTE:** Refer to text on specific vaccines or toxoids for indications, contraindications, precautions, dosages, side effects and adverse reactions, and special considerations.

\*Diphtheria and tetanus toxoids adsorbed (for adult use), Td, a combined preparation containing less than 2 Lf of diphtheria toxoid.

<sup>†</sup>Indicated for persons born after 1956.

<sup>§</sup>Indicated especially for susceptible males.

<sup>¶</sup>Principally recommended for females up to 45 years of age.



**TABLE 2. Immunobiologics recommended for special occupations, lifestyles, environmental circumstances, travel, foreign students, immigrants, and refugees\***

| Indication  | Immunobiologic(s)   |
|---|---|
| Occupation  |   |
| Hospital, laboratory, and other health care personnel | Hepatitis B<br>Polio<br>Influenza   |
| Staff of institutions for the mentally retarded       | Hepatitis B   |
| Veterinarians and animal handlers                     | Rabies  |
| Selected field workers                                | Plague  |
| Lifestyles  |   |
| Homosexual males                                      | Hepatitis B   |
| Illicit drug users                                    | Hepatitis B   |
| Environmental situation                               |   |
| Inmates of long-term correctional facilities          | Hepatitis B   |
| Residents of institutions for the mentally retarded   | Hepatitis B   |
| Travel  |   |
|   | Measles<br>Rubella<br>Polio<br>Yellow fever<br>Hepatitis B<br>Rabies<br>Meningococcal polysaccharide<br>Typhoid<br>Cholera<br>Plague<br>Immune globulin |
| Foreign students, immigrants, and refugees            | Measles<br>Rubella<br>Diphtheria<br>Tetanus   |

**NOTE:** Refer to text on specific vaccines or toxoids for use by specific risk groups, details on indications, contraindications, precautions, dosages, side effects and adverse reactions, and special considerations.

\*Unless specifically contraindicated, the vaccine or toxoids generally recommended for adults are also indicated. Table 1 shows vaccines and toxoids appropriate for age for most adults.

**TABLE 3. Vaccines and toxoids indicated or specifically contraindicated for special health status situations\***

| Health situations                         | Vaccines or toxoids   |                     |
|---|---|---------------------|
|   | Indicated   | Contraindicated     |
| Pregnancy                                 | Diphtheria and tetanus toxoids (Td)                                   | Live-virus vaccines |
| Immunocompromised                         | Influenza<br>Pneumococcal polysaccharide                              | Live-virus vaccines |
| Splenic dysfunction,<br>anatomic asplenia | Influenza<br>Pneumococcal polysaccharide                              |                     |
| Hemodialysis                              | Hepatitis B (double dose)<br>Influenza<br>Pneumococcal polysaccharide |                     |
| Deficiencies of<br>factors VIII or IX     | Hepatitis B   |                     |
| Chronic alcoholism                        | Pneumococcal polysaccharide   |                     |
| Diabetes and other high-<br>risk diseases | Influenza<br>Pneumococcal polysaccharide                              |                     |

**NOTE:** Refer to text on specific vaccines or toxoids for details on indications, contraindications, precautions, dosages, side effects and adverse reactions, and special considerations.

\*Unless specifically contraindicated, the vaccines and toxoids generally recommended for adults are also indicated. Table 1 shows vaccines and toxoids appropriate for age for most adults.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)<sup>a†</sup>

| Immunobiologic generic name    | Primary schedule and booster (s)  | Indications  | Major precautions and contraindications <sup>b</sup>   | Special considerations  |
|--------------------------------|---|--|--|---|
| <b>TOXOIDS</b>                 |   |  |  |   |
| Tetanus-diphtheria toxoid (Td) | 2 doses intramuscularly (IM) 4 weeks apart; 3rd dose 6-12 months after 2nd dose; booster every 10 years | All adults   | Except in the first trimester, pregnancy is not a contraindication. History of a neurologic reaction or immediate hypersensitivity reaction following a previous dose. History of severe local reaction (Arthus-type) following previous dose. Such individuals should not be given further routine or emergency doses of Td for 10 years. | Tetanus prophylaxis in wound management (summarized in text on page 11S and in Table 5)   |
| <b>LIVE-VIRUS VACCINES</b>     |   |  |  |   |
| Measles live-virus vaccine     | 1 dose subcutaneously (SC); no booster  | All adults born after 1956 without documentation of live vaccine on or after 1st birthday or physician-diagnosed measles or laboratory evidence of immunity; persons born before 1957 are generally considered immune. Susceptible travelers | Pregnancy; immunocompromised persons <sup>1</sup> ; history of anaphylactic reactions following egg ingestion or receipt of neomycin (see text)  | Measles, mumps, rubella vaccine (MMR) is the vaccine of choice if recipients are likely to be susceptible to rubella and/or mumps as well as to measles. Persons vaccinated between 1963 and 1967 with a killed-measles vaccine, followed by live vaccine within 3 months or with a vaccine of unknown type should be revaccinated with live-measles-virus vaccine. |
| Mumps live-virus vaccine       | 1 dose SC; no booster   | All adults, particularly males, believed to be susceptible can be vaccinated. Most adults can be considered immune.  | Pregnancy; immunocompromised persons <sup>1</sup> ; history of anaphylactic reaction following egg ingestion or receipt of neomycin (see text)   | MMR is the vaccine of choice if recipients are likely to be susceptible to measles and rubella as well as to mumps.   |

Rubella live-virus vaccine

1 dose SC; no booster

Indicated for adults, both male and female, lacking documentation of live vaccine on or after 1st birthday or laboratory evidence of immunity, particularly women of child-bearing age and young adults who work or congregate in places such as hospitals, colleges, and the military. Susceptible travelers

Pregnancy; immunocompromised persons<sup>†</sup>; history of anaphylactic reaction following receipt of neomycin

Women pregnant when vaccinated or who become pregnant within 3 months of vaccination should be counseled on the theoretical risks to the fetus. The risk of rubella vaccine-associated malformations in these women is so small as to be negligible. MMR is vaccine of choice if recipients are likely to be susceptible to measles or mumps as well as to rubella.

Smallpox vaccine (vaccinia virus)

THERE ARE NO INDICATIONS FOR THE USE OF SMALLPOX VACCINE IN THE GENERAL CIVILIAN POPULATION.

Laboratory workers involved with orthopox virus or in the production and testing of smallpox vaccines should receive regular smallpox vaccinations. For advice on vaccine administration and contraindications, contact the International Health Program Office, CDC, Atlanta, Georgia 30333.

Yellow fever live, attenuated virus (17D strain)

1 dose SC 6 days to 10 years before travel; booster every 10 years

Selected persons traveling or living in areas where yellow fever infection exists.

Although specific information is not available concerning adverse effects on the developing fetus,

Some countries require a valid International Certification of Vaccination showing receipt of vaccine.

<sup>\*</sup>Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

<sup>†</sup>Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezuelan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

<sup>§</sup>When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

<sup>¶</sup>Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)\*†—Continued

| Immunobiologic generic name  | Primary schedule and booster(s)  | Indications   | Major precautions and contraindications <sup>§</sup>  | Special considerations   |
|--|--|---|---|--|
| <b>LIVE-VIRUS AND INACTIVATED-VIRUS VACCINES</b>   |  |   |   |  |
| <p>Polio vaccines:<br/>Killed-poliovirus vaccine (IPV)<br/>Live-poliovirus vaccine (OPV)</p> | <p>IPV preferred for primary vaccination; 3 doses SC 4 weeks apart; a 4th dose 6-12 months after 3rd; for adults with a completed primary series and for whom a booster is indicated, either OPV or IPV can be given. If immediate protection is needed, OPV is recommended.</p> | <p>Persons traveling to areas where wild poliovirus is epidemic or endemic and certain health-care personnel (see text for recommendations for incompletely immunized adults and adults in households of children to be immunized).</p> | <p>it is prudent on theoretical grounds to avoid vaccinating pregnant women unless the individual must travel to areas where the risk of yellow fever is high. Immunocompromised persons; history of hypersensitivity to egg ingestion</p> <p>Although there is no convincing evidence documenting adverse effects of either OPV or IPV on the pregnant woman or developing fetus, it is prudent on theoretical grounds to avoid vaccinating pregnant women. However, if immediate protection against poliomyelitis is needed, OPV is recommended.</p> <p>OPV should not be given to immunocompromised individuals or to persons with known or possibly immunocompromised family members. IPV is recommended in such situations</p> | <p>If the only reason to vaccinate a pregnant woman is an international requirement, efforts should be made to obtain a waiver letter (see page 19S).</p> <p>Although a protective immune response to IPV in the immunocompromised individual cannot be assured, the vaccine is safe and some protection may result from its administration.</p> |
| <b>INACTIVATED-VIRUS VACCINES</b>  |  |   |   |  |
| <p>Hepatitis B (HB) inactivated-virus vaccine</p>  | <p>2 doses IM 4 weeks apart; 3rd dose 5 months after 2nd; need for boosters unknown</p>  | <p>Adults at increased risk of occupational, environmental, social, or family exposure</p>  | <p>Data are not available on the safety of the vaccine for the developing fetus. Because the vaccine</p>  | <p>The vaccine produces neither therapeutic nor adverse effects on HBV-infected persons. Prevacination serologic</p>   |

|  |  |  |   |  |
|--|--|--|---|--|
|  |  |  | contains only noninfectious hepatitis B surface antigen particles, the risk should be negligible. Pregnancy should <i>not</i> be considered a vaccine contraindication if the woman is otherwise eligible.  | screening for susceptibility before vaccination may or may not be cost effective depending on costs of vaccination and testing and on the prevalence of immune individuals in the group.                             |
| Influenza vaccine (inactivated whole-virus and split-virus) vaccine                | Annual vaccination with current vaccine. Either whole- or split-virus vaccine may be used.   | Adults with high-risk conditions, residents of nursing homes or other chronic-care facilities, medical-care personnel, healthy persons over 65.  | Although no evidence exists of maternal or fetal risk when vaccine is given in pregnancy because of an underlying high-risk condition in a pregnant woman, waiting until the second or third trimester, if possible, is reasonable. History of anaphylactic hypersensitivity to egg ingestion |  |
| Human diploid cell rabies vaccine (HDCV) (inactivated, whole-virion and subvirion) | Preexposure prophylaxis: 2 doses 1 week apart; 3rd dose 3 weeks after 2nd; if exposure continues, booster doses every 2 years, or an antibody titer determined | Veterinarians, animal handlers, certain laboratory workers, and persons living in or visiting countries for > 1 month where rabies is a constant | If there is substantial risk of exposure to rabies, preexposure vaccination may be indicated during pregnancy. Corticosteroids and immunosuppressive agents can interfere with  | Complete preexposure prophylaxis does not eliminate the need for additional therapy with rabies vaccine after a rabies exposure. The Food and Drug Administration has not approved the intradermal (ID) use of HDCV. |

\*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezuelan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

‡When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

§Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)\*†—Continued

| Immunobiologic generic name | Primary schedule and booster(s)   | Indications | Major precautions and contraindications <sup>§</sup>   | Special considerations   |
|-----------------------------|---|-------------|--|--|
|                             | <p>and a booster dose given if titer inadequate (&lt; 5)</p> <p>Postexposure prophylaxis: All postexposure treatment should begin with immediate cleansing of the wound with soap and water.</p> <p>(1) Persons who have</p> <p>a) previously received postexposure prophylaxis with HDCV, b) received recommended IM pre-exposure series of HDCV, c) received recommended ID preexposure series of HDCV in the U.S., or d) have a previously documented rabies antibody titer considered adequate: 2 doses of HDCV, 1.0 ml IM, one each on days 0 and 3</p> <p>(2) Persons not previously immunized as above: HRIG 20 international units (IU)/kg body weight, half infiltrated at bite site if possible, remainder IM; and 5 doses of HDCV, 1.0 ml-IM, one each on days 0, 3, 7, 14, 28</p> | threat      | the development of active immunity; history of anaphylactic or Type III hypersensitivity reaction to previous dose of HDCV (See text). | <p>Recommendations for the ID use of HDCV are currently being discussed. Suggestions concerning ID use of HDCV for preexposure prophylaxis are found on page 26S and in CDC. Rabies Prevention—United States, 1984. MMWR 1984;33: 393-402,407-8.</p> <p>The decision for postexposure use of HDCV depends on the species of biting animal, the circumstances of biting incident, and the type of exposure (i.e. bite, saliva contamination of wound, etc.). The type of and schedule for post-exposure prophylaxis depends upon the person's previous rabies vaccination status, or the result of a previous or current serologic test for rabies antibody. For post-exposure prophylaxis, HDCV should always be administered IM, <i>not</i> ID.</p> |

## INACTIVATED-BACTERIA VACCINES

|  |  |  |   |   |
|--|--|--|---|---|
| Cholera vaccine  | Two 0.5-ml doses SC or IM or two 0.2-ml doses ID 1 week to 1 month apart; booster doses (0.5 ml IM or 0.2 ml ID) every 6 months                                      | Travelers to countries requiring evidence of cholera vaccination for entry   | No specific information on vaccine safety during pregnancy. Use in pregnancy should reflect actual increased risk. Persons who have had severe local or systemic reactions to a previous dose   | One dose generally satisfies International Health Regulations. Some countries may require evidence of a complete primary series or a booster dose given within 6 months before arrival. Vaccination should not be considered as an alternative to continued careful selection of foods and water. |
| Meningococcal polysaccharide vaccines (bivalent A and C and tetravalent A, C, W135, and Y) | 1 dose in volume and by route specified by manufacturer; need for boosters unknown   | Travelers visiting areas of a country that are recognized as having epidemic meningococcal disease   | Pregnancy, unless there is substantial risk of infection  |   |
| Plague vaccine   | 3 IM doses; first dose 1.0 ml; 2nd dose 0.2 ml 1 month later; 3rd dose 0.2 ml 5 months after 2nd; booster doses (0.2 ml) at 1-2 year intervals if exposure continues | Selected travelers to countries reporting cases, for whom avoidance of rodents and fleas is impossible; all laboratory and field personnel working with <i>Yersinia pestis</i> organisms possibly resistant to antimicrobials; those engaged in <i>Y. pestis</i> aerosol experiments or in field operations in areas with enzootic | Pregnancy, unless there is substantial and unavoidable risk of exposure; persons with known hypersensitivity to any of the vaccine constituents (see manufacturer's label); patients who have had severe local or systemic reactions to a previous dose | Prophylactic antibiotics may be recommended for definite exposure whether or not the exposed persons has been vaccinated.   |

\*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezuelan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

‡When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.



TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)\*†—Continued

| Immunobiologic generic name                     | Primary schedule and booster(s)   | Indications   | Major precautions and contraindications <sup>b</sup>   | Special considerations  |
|---|---|---|--|---|
|   |   | plague where regular exposure to potentially infected wild rodents, rabbits, or their fleas cannot be prevented   |  |   |
| Pneumococcal polysaccharide vaccine (23 valent) | 1 dose, booster not recommended   | Adults who are at increased risk of pneumococcal disease and its complications because of underlying health conditions; older adults, especially those age 65 and over, who are healthy             | The safety of vaccine in pregnant women has not been evaluated; it should not be given during pregnancy unless the risk of infection is high. Previous recipients of any type of pneumococcal polysaccharide vaccine should not receive another dose of vaccine. |   |
| Typhoid vaccine                                 | Two 0.5-ml doses SC 4 or more weeks apart, booster 0.5 ml SQ or 0.1 ml ID every 3 years if exposure continues | Travelers to areas where there is a recognized risk of exposure to typhoid  | Severe local or systemic reaction to a previous dose. Acetone killed and dried vaccines should not be given ID.  | Vaccination should not be considered as an alternative to continued careful selection of foods and water.   |
| <b>LIVE-BACTERIA VACCINE</b>                    |   |   |  |   |
| BCG   | 1 ID or SC dose (see package label)   | Prolonged close contact with untreated or ineffectively treated active tuberculosis patients; groups with excessive rates of new infection in which other control measures have not been successful | Pregnancy, unless there is unavoidable exposure to infective tuberculosis; immunocompromised patients <sup>c</sup>   | In the United States tuberculosis control efforts are directed toward early identification, treatment of cases and preventive therapy with isoniazid. |
| <b>IMMUNE GLOBULINS</b>                         |   |   |  |   |
| Immune globulin (IG)                            | Hepatitis A prophylaxis<br>Preexposure-1 IM dose  | Household and sexual contacts of persons with   |  | For travelers IG is not an alternative to continued   |

of 0.02 ml/kg for anticipated risk of 2-3 months; IM dose of 0.06 ml/kg for anticipated risk of 5 months; repeat appropriate dose at above intervals if exposure continues.

Postexposure-1 IM dose of 0.02 ml/kg given within 2 weeks of exposure

Measles prophylaxis: 0.25 ml/kg IM (maximum 15 ml) given within 6 days after exposure

Hepatitis B immune globulin (HBIG) 0.06 ml/kg IM as soon as possible after exposure followed by a second dose 1 month later except when HB vaccine is given

hepatitis A; travelers to high-risk areas outside tourist routes; staff, attendees, and parents of diapered attendees in day-care-center outbreaks

Exposed susceptible contacts of measles cases

Following percutaneous or mucous membrane exposure to blood known to be HBsAg positive; following sexual exposure to or a bite from a person with acute HBV or an HBV carrier.

IG should *not* be used to control measles

Careful selection of foods and water. Frequent travelers should be tested for hepatitis antibody.

IG given within 6 days after exposure can prevent or modify measles. Recipients of IG for measles prophylaxis should receive live-measles vaccine 3 months later.

IG (0.06 ml/kg) may be used if HBIG is not available.

\*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

<sup>†</sup>Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezuelan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

<sup>§</sup>When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

<sup>¶</sup>Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation.

TABLE 4. Immunobiologics and schedules for adults (18 years of age and older)\*†—Continued

| Immunobiologic generic name             | Primary schedule and booster (s)                                      | Indications   | Major precautions and contraindications <sup>§</sup> | Special considerations  |
|---|---|---|--|---|
| Tetanus immune globulin (TIG)           | 250 units IM  | Part of management of nonclean, nonminor wound in a person with unknown tetanus toxoid status, with less than two previous doses, or with two previous doses and a wound more than 24 hours old.        |  |   |
| Rabies immune globulin, human (HRIG)    | 20 IU/kg, up to half infiltrated around wound, remainder IM           | Part of management of rabies exposure in persons lacking a history of recommended preexposure or postexposure prophylaxis with HDCV   |  | Although preferable to be given with the 1st dose of vaccine, can be given up to the 8th day after the 1st dose of vaccine. |
| Varicella-zoster immune globulin (VZIG) | Persons $\leq$ 50 kg: 125 units/10kg IM; persons > 50 kg: 625 units** | Immunocompromised patients known or likely to be susceptible with close and prolonged exposure to a household contact case or to an infectious hospital staff member or hospital roommate. <sup>¶</sup> |  |   |

NOTE: Refer to text on specific vaccines or toxoids for further details on indications, contraindications, precautions, dosages, side effects, and adverse reactions, and special considerations and individual ACIP statements (see list of published ACIP statements in Appendix 2).

\*Several other vaccines, toxoids, and immune globulins are licensed and available. These are noted in Appendix 3. In addition, the following antitoxins are licensed and available: (1) botulism antitoxin, trivalent (ABE) equine (distributed by CDC only), (2) tetanus antitoxin (equine), (3) diphtheria antitoxin (equine), and (4) rabies antitoxin (equine).

†Several vaccines and toxoids are in "Investigation of New Drug" (IND) status and available only through the Division of Host Factors, Center for Infectious Disease, CDC. These are: (1) pentavalent (ABCDE) botulinum toxoid, (2) eastern equine encephalitis (EEE) vaccine, (3) Venezuelan equine encephalitis (VEE) vaccine, and (4) tularemia vaccine

§When any vaccine or toxoid is indicated during pregnancy, waiting until the second or the third trimester, when possible, is a reasonable precaution that minimizes concern about teratogenicity.

¶Persons immunocompromised because of immune deficiency diseases, leukemia, lymphoma or generalized malignancy or immunosuppressed as a result of therapy with corticosteroids, alkylating drugs, antimetabolites or radiation.

\*\*Some persons have recommended 125 units/10 kg regardless of total body weight.

**TABLE 5. Summary guide to tetanus prophylaxis in routine wound management**

| History of tetanus immunization (doses) | Clean, minor wounds |      | All other wounds |                 |
|---|---------------------|------|------------------|-----------------|
|   | Td*                 | TIG† | Td*              | TIG†            |
| Uncertain                               | Yes                 | No   | Yes              | Yes             |
| 0-1                                     | Yes                 | No   | Yes              | Yes             |
| 2                                       | Yes                 | No   | Yes              | No <sup>§</sup> |
| 3 or more                               | No <sup>¶</sup>     | No   | No**             | No              |

NOTE: Refer to text on specific vaccines or toxoids for contraindications, precautions, dosages, side effects and adverse reactions, and special considerations. Important details are in the text and ACIP recommendation (MMWR 1981; 30:392-407).

\*The combined preparations Td, containing both tetanus and diphtheria toxoids, is preferred to tetanus toxoid alone.

†Tetanus immune globulin.

§Yes, if wound more than 24 hours old.

¶Yes, if more than 10 years since last dose.

\*\*Yes, if more than 5 years since last dose (more frequent boosters are not needed and can accentuate side effects.)

APPENDIX 1. Suggested immunization record form

Name \_\_\_\_\_ Sex \_\_\_\_\_ Birthdate \_\_\_\_\_

| VACCINE  | VACCINE TYPE | DATE GIVEN MO/DAY/YR | VACCINE LOT # | DOCTOR OR CLINIC | DATE DOSE DUE |
|--|--------------|----------------------|---------------|------------------|---------------|
| POLIO<br>OPV<br>or<br>IPV<br>(specify type used)   |              |                      |               |                  |               |
| DTP<br>(diphtheria tetanus pertussis)<br>DT<br>(Pediatric)<br>or<br>Td (Adult)<br>(specify type used)                |              |                      |               |                  |               |
| MEASLES<br>MUMPS<br>RUBELLA or<br>Combinations<br>(MMR,<br>measles-rubella,<br>rubella-mumps)<br>(specify type used) |              |                      |               |                  |               |
| OTHER<br>vaccines or<br>immune<br>globulins<br>(specify type used)   |              |                      |               |                  |               |
| TUBERCULIN TEST  |              |                      |               |                  |               |

NOTES:

APPENDIX 2. Published ACIP statements\* (as of June 30, 1984)

| Title of ACIP Statement  | MMWR Publication                             |
|--|--|
| General recommendations on immunizations   | 1983;32:1-8,13-7                             |
| Diphtheria, tetanus, and pertussis: guidelines for vaccine prophylaxis and other preventive measures | 1981;30:392-96,401-7<br>Erratum. 1981;30:420 |
| Measles prevention   | 1982;31:217-24,229-31                        |
| Mumps vaccine  | 1982;31:617-20,625                           |
| Rubella prevention   | 1984;33:301-10,315-8                         |
| Yellow fever vaccine   | 1984;32:679-82,687-8                         |
| Poliomyelitis prevention   | 1982;31:22-6,31-4                            |
| Prevention and control of influenza <sup>†</sup>   | 1984;33:253-60,265-6                         |
| Inactivated hepatitis B virus vaccine  | 1982;31:317-22,327-8                         |
| Postexposure prophylaxis of hepatitis B  | 1984;33:285-90                               |
| Rabies prevention<br>Supplementary statement on rabies vaccine and serologic testing                 | 1981;30:535-6                                |
| Rabies   | 1984;33:393-402,407-8                        |
| Supplementary statement on pre-exposure rabies prophylaxis by the intradermal route                  | 1982;31:279-80,285                           |
| Cholera vaccine  | 1978;27:173-4                                |
| Meningococcal polysaccharide vaccine   | 1978;27:327-9                                |
| Plague vaccine   | 1982;31:301-4                                |
| Update: Pneumococcal polysaccharide vaccine usage—United States                                      | 1984;33:273-6,81                             |
| Typhoid vaccine  | 1978;27:231-3                                |
| BCG vaccines   | 1979;28:241-4                                |
| Immune globulins for protection against viral hepatitis  | 1981;30:423-8,433-5                          |
| Varicella-zoster immune globulin for the prevention of chickenpox                                    | 1984;33:84-90,95-100                         |

\*The Immunization Practices Advisory Committee (ACIP) periodically reviews recommendations on vaccination and prophylaxis. When recommendations are revised, they are published individually in the MMWR.

<sup>†</sup>Each year influenza vaccine recommendations are reviewed and amended to reflect updated information on influenza activity in the United States for the preceding influenza season and to provide information on the vaccine available for the upcoming influenza season. These recommendations are published in the MMWR annually, usually during June or July.

**APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name**

| Immunobiologic  | Manufacturer  | Product Name  |
|---|---|---|
| Adenovirus vaccine  | Wyeth Labs, Inc   | Adenovirus, Live, Oral, Type 4*<br>Adenovirus, Live, Oral, Type 7*                                  |
| Anthrax vaccine   | Biol Prods Program,<br>Michigan Dept of<br>Public Health      | Anthrax Vaccine Adsorbed  |
| BCG vaccine   | Glaxo Operations UK<br>Limited                                | BCG Vaccine   |
|   | Inst Tuberculosis<br>Research, Univ Of<br>Illinois at Chicago | BCG Vaccine   |
| Cholera vaccine   | Lederle Laboratories,<br>Div American Cyanamid Co             | Cholera Vaccine (strains<br>Ogawa-Inaba)  |
|   | Wyeth Labs, Inc   | Cholera Vaccine   |
|   | Sclavo SpA <sup>†</sup>                                       | Cholera Vaccine   |
| Diphtheria and tetanus<br>toxoids adsorbed                          | Lederle Laboratories,<br>Div American Cyanamid Co             | Diphtheria Tetanus Toxoids<br>Adsorbed (Purogenated for<br>Pediatric Use)                           |
|   | Massachusetts Public<br>Health Biol Labs                      | Diphtheria and Tetanus Toxoids<br>Adsorbed  |
|   | Biol Prods Program,<br>Michigan Dept of<br>Public Health      | Diphtheria and Tetanus Toxoids<br>Adsorbed (Pediatric) <sup>§</sup>                                 |
|   | Sclavo SpA <sup>†</sup>                                       | Diphtheria and Tetanus Toxoids<br>Adsorbed (For Pediatric Use)                                      |
|   | Wyeth Labs, Inc   | Diphtheria and Tetanus Toxoids<br>Adsorbed ((pediatric) Aluminum<br>Phosphate Adsorbed, Ultrafined) |
| Diphtheria and tetanus<br>toxoids and pertussis<br>vaccine adsorbed | Connaught Labs, Inc <sup>†</sup>                              | Diphtheria and Tetanus Toxoids and<br>Pertussis Vaccine Adsorbed                                    |
|   | Lederle Laboratories,<br>Div American Cyanamid Co             | Diphtheria and Tetanus Toxoids and<br>Pertussis Vaccine Adsorbed<br>(Tri Immunol <sup>™</sup> )     |
|   | Massachusetts Public<br>Health Biol Labs                      | Diphtheria and Tetanus Toxoids and<br>Pertussis Vaccine Adsorbed                                    |

\*Available *only* to the U.S. Armed Forces.

<sup>†</sup>Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc.  
<sup>§</sup>Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued

| Immunobiologic                 | Manufacturer  | Product Name   |
|--------------------------------|---|--|
|                                | Biol Prods Program,<br>Michigan Dept of<br>Public Health                          | Diphtheria and Tetanus Toxoids and<br>Pertussis Vaccine Adsorbed <sup>§</sup>  |
|                                | Wyeth Labs, Inc   | Diphtheria and Tetanus Toxoids and<br>Pertussis Vaccine Adsorbed<br>(Aluminum Phosphate Adsorbed,<br>Ultrafined, Triple Antigen) |
| Diphtheria toxoid adsorbed     | Sclavo SpA <sup>†</sup>   | Diphtheria Toxoid Adsorbed<br>(Pediatric)  |
| Hepatitis B immune<br>globulin | Alpha Therapeutic Corp<br>Produces for<br>Abbott Laboratories                     | Hepatitis B Immune Globulin<br>(Human) (H-BIG <sup>®</sup> )   |
|                                | Merck Sharp & Dohme Div<br>of Merck & Co, Inc                                     | Hepatitis B Immune Globulin (Human)<br>(MSD, HEP-B-GAMMEE <sup>®</sup> )   |
|                                | Cutter Biological Div<br>of Miles Labs, Inc                                       | Hepatitis B Immune Globulin<br>(HYPER-HEP <sup>®</sup> )   |
| Hepatitis B vaccine            | Merck Sharp & Dohme Div<br>of Merck & Co, Inc                                     | Hepatitis B Vaccine (MSD,<br>HEPTAVAX-B <sup>®</sup> )   |
| Immune globulin                | Alpha Therapeutic Corp  | Immune Serum Globulin (Human)  |
|                                | Armour Pharmaceutical<br>Co   | Immune Serum Globulin (Human)<br>(GAMMAR <sup>®</sup> )  |
|                                | Central Laboratory Blood<br>Transfusion Service, Swiss<br>Red Cross               | Immune Globulin Intravenous<br>(SANDOGLOBULIN <sup>®</sup> )   |
|                                | Cutter Biological Div<br>of Miles Labs, Inc                                       | Immune Serum Globulin (Human)<br>(GAMASTAN <sup>®</sup> )  |
|                                |   | Immune Globulin Intravenous<br>[5% in 10% Maltose (GAMIMUNE <sup>®</sup> )]  |
|                                | Hyland Therapeutics Div<br>Travenol Labs, Inc<br>also produces for<br>Savage Labs | Immune Serum Globulin (Human)  |
|                                |   | Immune Serum Globulin (Human)<br>(IMMUGLOBULIN <sup>®</sup> )  |
|                                | Massachusetts Public<br>Health Biol Labs  | Immune Serum Globulin (Human)  |

<sup>†</sup>Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

<sup>§</sup>Outside of Michigan, available only to health departments.



APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued

| Immunobiologic                          | Manufacturer   | Product Name  |
|---|--|---|
|   | Biol Prods Program,<br>Michigan Dept of<br>Public Health | Immune Serum Globulin (Human)   |
|   | Wyeth Labs, Inc  | Immune Serum Globulin (Human)   |
|   | New York Blood Ctr, Inc                                  | Immune Serum Globulin (Human)   |
| Influenza vaccine                       | Connaught Labs, Inc <sup>†</sup>                         | Influenza Virus Vaccine<br>([Zonal Purified]), Whole Virion<br>(FLUZONE <sup>®</sup> )      |
|   |  | Influenza Virus Vaccine<br>([Zonal Purified]), Split Virion<br>(FLUZONE <sup>®</sup> )      |
|   | Parke-Davis, Div of<br>Warner-Lambert Co                 | Influenza Virus Vaccine<br>(Split Virion [FLUOGEN <sup>®</sup> ])                           |
|   | Wyeth Labs, Inc  | Influenza Virus Vaccine<br>Trivalent Types A and B<br>(Chromatograph),<br>Subvirion Antigen |
| Measles and mumps<br>vaccine, live      | Merck Sharp & Dohme Div<br>of Merck & Co, Inc            | Measles and Mumps Virus Vaccine,<br>Live (MSD, M-M-VAX <sup>™</sup> )                       |
| Measles, mumps and rubella<br>vaccine   | Merck Sharp & Dohme Div<br>of Merck & Co, Inc            | Measles, Mumps and Rubella<br>Virus Vaccine, Live<br>(MSD, MMR II <sup>-</sup> )            |
| Measles and rubella vaccine             | Merck Sharp & Dohme Div<br>of Merck & Co, Inc            | Measles and Rubella Virus<br>Vaccine, Live<br>(MSD, M-R-VAX II <sup>-</sup> )               |
| Measles vaccine                         | Merck Sharp & Dohme Div<br>of Merck & Co, Inc            | Measles Virus Vaccine, Live<br>(Attenuated [MSD,<br>ATTENUVAX <sup>™</sup> ])               |
| Meningococcal polysaccharide<br>vaccine |  |   |
| A and C                                 | Connaught Labs, Inc <sup>†</sup>                         | Meningococcal<br>Polysaccharide Vaccine<br>(MENOMUNE-A/C <sup>-</sup> )                     |
| A, C, Y, and W 135                      | Connaught Labs, Inc <sup>†</sup>                         | Meningococcal<br>Polysaccharide Vaccine<br>(MENOMUNE-A/CY'W-135 )                           |

<sup>†</sup>Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

**APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued**

| Immunobiologic                    | Manufacturer  | Product Name  |
|-----------------------------------|---|---|
| Mumps vaccine                     | Merck Sharp & Dohme Div of Merck & Co, Inc          | Mumps Virus Vaccine, Live (MSD, MUMPSVAX <sup>®</sup> )                             |
| Pertussis immune globulin         | Cutter Biological Div of Miles Labs, Inc            | Pertussis Immune Globulin (Human) (HYPERTUSSIS <sup>™</sup> )                       |
| Pertussis vaccine adsorbed        | Biol Prods Program, Michigan Dept of Public Health  | Pertussis Vaccine Adsorbed  |
| Plague vaccine                    | Cutter Biological Div of Miles Labs, Inc            | Plague Vaccin <sup>o</sup>  |
| Pneumococcal polysaccharide       | Lederle Laboratories, Div American Cyanamid Co      | Pneumococcal Vaccine, Polyvalent (PNEU-IMUNE23 <sup>™</sup> )                       |
|                                   | Merck Sharp & Dohme Div of Merck & Co, Inc          | Pneumococcal Vaccine, Polyvalent (MSD, PNEUMOVAX 23 <sup>™</sup> )                  |
| Poliovirus vaccine<br>Inactivated | Connaught Labs, Ltd <sup>†</sup><br>(Purified-Salk) | Poliomyelitis Vaccine   |
|                                   | Oral  | Lederle Laboratories, Div American Cyanamid Co                                      |
| Rabies immune globulin            | Cutter Biological Div of Miles Labs, Inc            | Rabies Immune Globulin (Human) (HYPERAB <sup>™</sup> )                              |
|                                   | Institut Merieux <sup>†</sup>                       | Rabies Immune Globulin (Human) (IMOGAMRABIES <sup>™</sup> )                         |
| Rabies vaccine                    | Institut Merieux <sup>†</sup>                       | Rabies Vaccine (Human Diploid Cell [IMOVAX <sup>™</sup> ])                          |
|                                   | Wyeth Labs, Inc                                     | Rabies Vaccine (Human Diploid Cell Strain, Subvirion Antigen [WYVAC <sup>™</sup> ]) |
| Rubella vaccine                   | Merck Sharp & Dohme Div of Merck & Co, Inc          | Rubella Virus Vaccine, Live (MSD, MERUVAX <sup>™</sup> II)                          |
| Rubella and mumps vaccine         | Merck Sharp & Dohme Div of Merck & Co, Inc          | Rubella and Mumps Virus Vaccine, Live (MSD, BIAVAX <sup>™</sup> II)                 |
| Tetanus immune globulin           | Alpha Therapeutic Corp                              | Tetanus Immune Globulin (Human)   |

<sup>†</sup>Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

**APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued**

| Immunobiologic                             | Manufacturer  | Product Name  |
|--|---|---|
|  | Cutter Biological Div<br>of Miles Labs, Inc                                       | Tetanus Immune-Globulin (Human)<br>(HYPER-TET™)   |
|  | Hyland Therapeutics Div<br>Travenol Labs, Inc                                     | Tetanus Immune Globulin (Human)<br>(HU-TET®)  |
|  | Hyland Therapeutics Div<br>Travenol Labs, Inc<br>also produces for<br>Savage Labs | Tetanus Immune Globulin (Human)<br>(HOMO-TET™)  |
|  | Wyeth Labs, Inc   | Tetanus Immune Globulin (Human)   |
|  | Massachusetts Public<br>Health Biol Labs  | Tetanus Immune Globulin (Human)   |
| Tetanus and diphtheria<br>toxoids adsorbed | Connaught Labs, Inc†  | Tetanus and Diphtheria Toxoids<br>Adsorbed (For Adult Use)  |
|  | Lederle Laboratories,<br>Div American Cyanamid Co                                 | Tetanus and Diphtheria Toxoids<br>Adsorbed (For Adult Use)<br>(Purogenated Parenteral)                                  |
|  | Massachusetts Public<br>Health Biol Labs  | Tetanus and Diphtheria Toxoids<br>Adsorbed (For Adult Use)  |
|  | Biol Prods Program,<br>Michigan Dept of<br>Public Health                          | Tetanus and Diphtheria Toxoids<br>Adsorbed (For Adult Use) (not<br>available to health departments<br>outside Michigan) |
|  | Sclavo SpA†   | Tetanus and Diphtheria Toxoids<br>Adsorbed (For Adult Use)  |
|  | Wyeth Labs, Inc   | Tetanus and Diphtheria Toxoids<br>Adsorbed (For Adult Use)<br>[Aluminum Phosphate, Ultrafined]                          |
| Tetanus toxoid adsorbed                    | Connaught Labs, Inc†  | Tetanus Toxoid Adsorbed   |
|  | Lederle Laboratories,<br>Div American Cyanamid Co                                 | Tetanus Toxoid Adsorbed<br>(Purogenated [Aluminum Phosphate<br>Adsorbed])   |
|  | Massachusetts Public<br>Health Biol Labs  | Tetanus Toxo'id Adsorbed  |

†Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

**APPENDIX 3. Immunobiologics available as of June 30, 1984, by manufacturer and product name — Continued**

| Immunobiologic                      | Manufacturer   | Product Name  |
|-------------------------------------|--|---|
|                                     | Biol Prods Program,<br>Michigan Dept of<br>Public Health | Tetanus Toxoid Adsorbed   |
|                                     | Sclavo SpA <sup>†</sup>                                  | Tetanus Toxoid Adsorbed   |
|                                     | Wyeth Labs, Inc  | Tetanus Toxoid Adsorbed<br>(Aluminum Phosphate Adsorbed,<br>Ultrafined)       |
| Tetanus toxoid, fluid               | Connaught Labs, Inc <sup>†</sup>                         | Tetanus Toxoid (Fluid)  |
|                                     | Lederle Laboratories,<br>Div American Cyanamid Co        | Tetanus Toxoid<br>(Purogenated, Tetanus Toxoid Fluid)                         |
|                                     | Wyeth Labs, Inc  | Tetanus Toxoid<br>(Fluid, Purified, Ultrafined)                               |
| Typhoid vaccine                     | Wyeth Labs, Inc  | Typhoid Vaccine <sup>¶</sup>  |
| Varicella-zoster immune<br>globulin | Massachusetts Public<br>Health Biol Labs                 | Varicella-Zoster Immune Globulin<br>(Human)                                   |
| Yellow fever vaccine                | Connaught Labs, Inc <sup>†</sup>                         | Yellow Fever Vaccine<br>(Live, 17D Virus, ALV-Free<br>[YF-VAX <sup>®</sup> ]) |

**NOTE:** In the preparation of this appendix every effort was made to assure its completeness and accuracy. This appendix was compiled from information obtained from manufacturers, the Division of Product Certification, Food and Drug Administration, and the Physicians Desk Reference, 37th Edition, 1983, and to the best of our knowledge is an accurate and complete listing as of June 30, 1984. However, omissions and errors may have occurred inadvertently. This appendix is intended to be a resource and does not replace the provider's obligation to remain otherwise current on the availability of vaccines, toxoids, and immune globulins.

<sup>†</sup>Connaught Laboratories, Inc., products distributed in the United States by E. R. Squibb and Sons, Inc. Sclavo SpA products distributed in United States by Sclavo, Inc. Institut Merieux products distributed in United States by Merieux Institute, Inc.

<sup>¶</sup>The acetone-killed and -dried form of this vaccine is available only to the U.S. Armed Forces.

APPENDIX 4. Use of immunobiologics in pregnancy<sup>a†</sup>

| Immunizing agent           | Risk from disease to pregnant female   | Risk from disease to fetus or neonate  | Type of immunizing agent  | Risk from immunizing agent to fetus | Indications for immunization during pregnancy  | Dose schedule   | Comments   |
|----------------------------|--|--|---|-------------------------------------|--|---|--|
| <b>LIVE-VIRUS VACCINES</b> |  |  |   |                                     |  |   |  |
| Measles                    | Significant morbidity, low mortality; not altered by pregnancy               | Significant increase in abortion rate; may cause malformations   | Live, attenuated virus vaccine  | None confirmed                      | Contraindicated (See immune globulins)   | Single dose   | Vaccination of susceptible women should be part of post-partum care  |
| Mumps                      | Low morbidity and mortality; not altered by pregnancy                        | Probable increased rate of abortion in 1st trimester. Questionable association of fibroelastosis in neonates | Live, attenuated virus vaccine  | None confirmed                      | Contraindicated  | Single dose   |  |
| Poliomyelitis              | No increased incidence in pregnancy, but may be more severe if it does occur | Anoxic fetal damage reported; 50% mortality in neonatal disease  | Live, attenuated virus (OPV) and inactivated virus (IPV) vaccine <sup>b</sup> | None confirmed                      | Not routinely recommended for adults in U.S., except persons at increased risk of exposure | Primary: 3 doses of IPV at 4-8 week intervals and a 4th dose 6-12 months after the 3rd dose; 2 doses of OPV with a 6-8 week interval and a 3rd dose at least 6 weeks later, customarily 8-12 months later. Booster: Every 5 years until 18 years of age for IPV | Vaccine indicated for susceptible pregnant women traveling in endemic areas or in other high-risk situations |

|                                      |   |  |   |                |  |  |  |
|--------------------------------------|---|--|---|----------------|--|--|--|
| Rubella                              | Low morbidity and mortality; not altered by pregnancy                                     | High rate of abortion and congenital rubella syndrome                | Live, attenuated virus vaccine  | None confirmed | Contraindicated  | Single dose  | Teratogenicity of vaccine is theoretical, not confirmed to date; vaccination of susceptible women should be part of post-partum care |
| Yellow fever                         | Significant morbidity and mortality; not altered by pregnancy                             | Unknown  | Live, attenuated virus vaccine  | Unknown        | Contraindicated except if exposure unavoidable             | Single dose  | Postponement of travel preferable to vaccination, if possible  |
| <b>TOXOIDS</b>                       |   |  |   |                |  |  |  |
| Tetanus-Diphtheria                   | Severe morbidity; tetanus mortality 60%, diphtheria mortality 10%; unaltered by pregnancy | Neonatal tetanus mortality 60%                                       | Combined tetanus-diphtheria toxoids preferred; adult tetanus-diphtheria formulation | None confirmed | Lack of primary series, or no booster within past 10 years | Primary: 2 doses at 1- to 2-month interval with a 3rd dose 6-12 months after the second; Booster: single dose every 10 years, after completion of the primary series | Updating of immune status should be part of antepartum care  |
| <b>IMMUNE GLOBULINS: HYPERIMMUNE</b> |   |  |   |                |  |  |  |
| Hepatitis B                          | Possible increased severity during 3rd trimester  | Possible increase in abortion rate and prematurity. Perinatal trans- | Hepatitis B immune globulin (HBIG)  | None reported  | Postexposure prophylaxis                                   | 0.06 ml/kg or 5 ml immediately, plus hepatitis B (HB) vaccine series, if indicated   | Infants born to HBsAg-positive mothers should receive 0.5 ml HBIG as soon as   |

\*Reproduced from: American College of Obstetrics and Gynecologists. Immunization during pregnancy (ACOG Technical Bulletin #64), Washington, D.C. ACOG. May 1982.

†The Appendix, Immunization During Pregnancy, describes methods and techniques of clinical practice that are currently acceptable and used by recognized authorities. However, it does not represent official policy or recommendations of the American College of Obstetricians and Gynecologists. Its publication should not be construed as excluding other acceptable methods of handling similar problems.

‡IPV recommended for unimmunized adults at increase risk.

## APPENDIX 4. Use of immunobiologics in pregnancy\*† — Continued

| Immunizing agent                  | Risk from disease to pregnant female             | Risk from disease to fetus or neonate   | Type of immunizing agent                | Risk from immunizing agent to fetus | Indications for immunization during pregnancy                          | Dose schedule                                 | Comments   |
|-----------------------------------|--|---|---|-------------------------------------|--|---|--|
|                                   |  | mission may occur if mother is a chronic carrier or is acutely infected   |   |                                     |  |   | possible after birth, plus 0.5 ml HB vaccine within 1 week of birth. Vaccine should be repeated at 1 and 6 months  |
| Rabies                            | Near 100% fatality; not altered by pregnancy     | Determined by maternal disease  | Rabies immune globulin (RIG)            | None reported                       | Postexposure prophylaxis   | 20 IU/kg in one dose of RIG                   | Used in conjunction with rabies killed-virus vaccine   |
| Tetanus                           | Severe morbidity; mortality 60%                  | Neonatal tetanus mortality 60%  | Tetanus immune globulin (TIG)           | None reported                       | Postexposure prophylaxis   | 250 units in one dose of TIG                  | Used in conjunction with tetanus toxoid  |
| Varicella                         | Possible increase in severe varicella pneumonia  | Can cause congenital varicella with increased mortality in neonatal period; very rarely causes congenital defects | Varicella-zoster immune globulin (VZIG) | None reported                       | Not routinely indicated in healthy pregnant women exposed to varicella | 1 vial/kg in one dose of VZIG, up to 5 vials  | Only indicated for newborns of mothers who developed varicella within 4 days prior to delivery or 2 days following delivery. Approximately 90%-95% of adults are immune to varicella |
| <b>INACTIVATED-VIRUS VACCINES</b> |  |   |   |                                     |  |   |  |
| Hepatitis B                       | Possible increased severity during 3rd trimester | Possible increase in abortion rate and prematurity.   | Inactivated HB vaccine                  | None reported                       | Indications for prophylaxis not altered by pregnancy                   | 1.0 ml (20 µg) IM at time, 0, 1, and 6 months | Infants born to HBsAg-positive mothers should receive 0.5 ml   |

|                                      |  |  |  |                |  |   |   |
|--------------------------------------|--|--|--|----------------|--|---|---|
|                                      |  | Perinatal transmission may occur if mother is a chronic carrier or is acutely infected |  |                |  |   | HBIG as soon as possible after birth, plus 0.5 ml HB vaccine within 1 week of birth. Vaccine should be repeated at 1 and 6 months |
| Influenza                            | Possible increase in morbidity and mortality during epidemic of new antigenic strain | Possible increased abortion rate; no malformations confirmed                           | Inactivated type A and type B virus vaccines | None confirmed | Usually recommended only for patients with serious underlying diseases; public health authorities to be consulted for current recommendation | Consult with public health authorities since recommendations change each year | Criteria for vaccination of pregnant women same as for all adults   |
| Rabies                               | Near 100% fatality; not altered by pregnancy   | Determined by maternal disease   | Killed-virus vaccine                         | Unknown        | Indications for prophylaxis not altered by pregnancy; each case considered individually  | Public health authorities to be consulted for indications and dosage          |   |
| <b>INACTIVATED-BACTERIA VACCINES</b> |  |  |  |                |  |   |   |
| Cholera                              | Significant morbidity and mortality; more severe during 3rd trimester                | Increased risk of fetal death during 3rd trimester maternal illness                    | Killed-bacteria vaccine                      | Unknown        | Only to meet international travel requirements   | 2 injections, 4-8 weeks apart   | Vaccine of low efficacy   |

\*Reproduced from: American College of Obstetrics and Gynecologists. Immunization during pregnancy (ACOG Technical Bulletin #64), Washington, D.C. ACOG, May 1982.

†The Appendix, Immunization During Pregnancy, describes methods and techniques of clinical practice that are currently acceptable and used by recognized authorities. However, it does not represent official policy or recommendations of the American College of Obstetricians and Gynecologists. Its publication should not be construed as excluding other acceptable methods of handling similar problems.



## APPENDIX 4. Use of immunobiologics in pregnancy\*† — Continued

| Immunizing agent | Risk from disease to pregnant female                                   | Risk from disease to fetus or neonate                        | Type of immunizing agent          | Risk from immunizing agent to fetus       | Indications for immunization during pregnancy   | Dose schedule  | Comments   |
|------------------|--|--|-----------------------------------|---|---|--|--|
| Meningo-coccus   | No increased risk during pregnancy; no increase in severity of disease | Unknown  | Killed-bacteria vaccine           | No data available on use during pregnancy | Indications not altered by pregnancy; vaccination recommended only in unusual outbreak situations | Public health authorities to be consulted                            |  |
| Plague           | Significant morbidity and mortality; not altered by pregnancy          | Determined by maternal disease                               | Killed-bacteria vaccine           | None reported                             | Very selective vaccination of exposed persons   | Public health authorities to be consulted for indications and dosage |  |
| Pneumo-coccus    | No increased risk during pregnancy; no increase in severity of disease | Unknown  | Polyvalent polysaccharide vaccine | No data available on use during pregnancy | Indications not altered by pregnancy; vaccine used only for high-risk individuals                 | In adults 1 dose only  |  |
| Typhoid          | Significant morbidity and mortality; not altered by pregnancy          | Unknown  | Killed-bacteria vaccine           | None confirmed                            | Not recommended routinely except for close, continued exposure or travel to endemic areas         | Primary; 2 injections, 4 weeks apart; Booster; single dose           |  |
| Hepatitis A      | Possible increased severity during 3rd trimester                       | Probable increase in abortion rate and prematurity. Possible | Pooled immune globulin (IG)       | None reported                             | Postexposure prophylaxis  | 0.02 ml/kg in 1 dose of IG   | IG should be given as soon as possible and within 2 weeks of |

transmission to neonate at delivery if mother is incubating the virus or is acutely ill at that time

exposure. Infants<sup>\*</sup> born to mothers who are incubating the virus or are acutely ill at delivery should receive one dose of 0.5 ml as soon as possible after birth

|         |  |  |                             |               |                          |   |  |
|---------|--|--|-----------------------------|---------------|--------------------------|---|--|
| Measles | Significant morbidity, low mortality; not altered by pregnancy | Significant increase in abortion rate; may cause malformations | Pooled immune globulin (IG) | None reported | Postexposure prophylaxis | 0.25 ml/kg in 1 dose of IG, up to 15 ml | Unclear if it prevents abortion. Must be given within 6 days of exposure |
|---------|--|--|-----------------------------|---------------|--------------------------|---|--|

\*Reproduced from: American College of Obstetrics and Gynecologists. Immunization during pregnancy (ACOG Technical Bulletin #64), Washington, D.C. ACOG. May 1982.

†The Appendix, Immunization During Pregnancy, describes methods and techniques of clinical practice that are currently acceptable and used by recognized authorities. However, it does not represent official policy or recommendations of the American College of Obstetricians and Gynecologists. Its publication should not be construed as excluding other acceptable methods of handling similar problems.

**APPENDIX 5. Varicella-zoster immune globulin—regional distribution centers**

| Service area              | Regional center and 24-hour telephone  | Service area  | Regional center and 24-hour telephone  |
|---------------------------|--|---|--|
| Massachusetts             | Massachusetts Public Health<br>Biologics Laboratories<br>305 South St.<br>Jamaica Plain, MA 02130<br>(617) 522-3700  |   | American Red Cross<br>Blood Services<br>Rochester Region<br>50 Prince St.<br>Rochester, NY 14607<br>(716) 461-9800                                 |
| Maine                     | American Red Cross<br>Blood Services<br>Northeast Region<br>812 Huntington Ave.<br>Boston, MA 02115<br>(617) 731-2130  |   | American Red Cross<br>Blood Services<br>Syracuse Region<br>636 S. Warren St.<br>Syracuse, NY 13202<br>(315) 425-1647                               |
|                           | American Red Cross<br>Blood Services<br>Northeast Region-<br>Portland Location<br>524 Forest Ave.<br>Portland, ME 04101<br>(207) 775-2367  | Delaware,<br>Pennsylvania,<br>Southern<br>New Jersey      | American Red Cross<br>Blood Services<br>Penn-Jersey Region<br>23rd and Chestnut<br>Philadelphia, PA 19103<br>(215) 299-4110                        |
| Connecticut               | American Red Cross<br>Blood Services<br>Connecticut Region<br>209 Farmington Ave.<br>Farmington, CT 06032<br>(203) 678-2730  | Maryland  | American Red Cross<br>Blood Services<br>Baltimore Region<br>2701 N. Charles St.<br>Baltimore, MD 21218<br>(301) 467-9905                           |
| Vermont,<br>New Hampshire | American Red Cross<br>Blood Services<br>Vermont-New Hampshire<br>Region<br>32 N. Prospect St.<br>Burlington, VT 05402<br>(802) 658-6400  | Virginia  | American Red Cross<br>Blood Services<br>Tidewater Region<br>611 W. Brambleton Ave.<br>P.O. Box 1836<br>Norfolk, VA 23501<br>(804) 446-7708         |
| Rhode Island              | Rhode Island Blood Center<br>551 N. Main St.<br>Providence, RI 02904<br>(401) 863-8368   |   | Richmond Metropolitan<br>Blood Service<br>2201 Westwood Ave.<br>Richmond, VA 23230<br>(804) 359-5100   |
| New Jersey,<br>New York   | The Greater New York<br>Blood Program<br>150 Amsterdam Ave.<br>New York, NY 10023<br>(212) 570-3067<br>(212) 570-3068 (night)  | Washington, D.C.,<br>Maryland, Virginia,<br>West Virginia | American Red Cross<br>Blood Services<br>Washington Region<br>2025 E Street, N.W.<br>Washington, DC 20006<br>(202) 728-6426                         |
| New York                  | American Red Cross<br>Blood Services<br>Northeastern New York Region<br>Hackett Blvd. at<br>Clara Barton Dr.<br>Albany, NY 12208<br>(518) 449-5020<br>(518) 462-7461<br>(518) 462-6964 (night) |   | American Red Cross<br>Blood Services<br>Tri-State Region<br>1111 Veterans Memorial Blvd.<br>F.O. Box 605<br>Huntington, WV 25710<br>(304) 522-0328 |
|                           | American Red Cross<br>Blood Services<br>Greater Buffalo Chapter<br>786 Delaware Ave.<br>Buffalo, NY 14209<br>(716) 886-7500  |   |  |

APPENDIX 5. Varicella-zoster immune globulin—regional distribution centers —  
Continued

| Service area            | Regional center and 24-hour telephone  | Service area                                      | Regional center and 24-hour telephone  |
|-------------------------|--|---|--|
| Georgia                 | American Red Cross<br>Blood Services<br>Atlanta Region<br>1925 Monroe Dr., N.E.<br>Atlanta, GA 30324<br>(404) 881-9800<br>(404) 881-6752 (night) |   | American Red Cross<br>Blood Services<br>Wolverine Region<br>202 E. Boulevard Dr.<br>Flint, MI 48501<br>(313) 232-1176                          |
| North Carolina          | American Red Cross<br>Blood Services<br>Carolinas Region<br>2425 Park Rd.<br>Charlotte, NC 28236<br>(704) 376-1661                               |   | American Red Cross<br>Blood Services<br>Great Lakes Region<br>1800 E. Grand River<br>Lansing, MI 48912<br>(517) 484-7461                       |
| South Carolina          | American Red Cross<br>Blood Services<br>South Carolina Region<br>1100 Shirley St.<br>Columbia, SC 29205<br>(803) 256-2301                        | Ohio  | American Red Cross<br>Blood Services<br>Northern Ohio Region<br>3950 Chester Ave.<br>Cleveland, OH 44114<br>(216) 781-1800                     |
| Florida                 | South Florida<br>Blood Service<br>1675 N.W. Ninth Ave.<br>Miami, FL 33136<br>(305) 326-8888  |   | American Red Cross<br>Central Ohio Region<br>995 E. Broad St.<br>Columbus, OH 43205<br>(614) 253-7981  |
|                         | American Red Cross<br>Blood Services<br>Mid-Florida Region<br>341 White St.<br>Daytona Beach, FL 32014<br>(904) 255-5444                         | Wisconsin, Iowa,<br>North Dakota,<br>South Dakota | The Blood Center of<br>S.E. Wisconsin<br>1701 W. Wisconsin Ave.<br>Milwaukee, WI 53233<br>(414) 933-5000                                       |
| Alabama,<br>Mississippi | American Red Cross<br>Blood Services<br>Alabama Region<br>2225 Third Ave., N.<br>Birmingham, AL 35203<br>(205) 322-5661                          | Wisconsin   | American Red Cross<br>Blood Services<br>Badger Region<br>1202 Ann St.<br>Madison, WI 53713<br>(608) 255-0021                                   |
| Indiana                 | American Red Cross<br>Blood Services<br>Fort Wayne Region<br>1212 E. California Rd.<br>Fort Wayne, IN 46825<br>(219) 482-3781                    | Minnesota   | American Red Cross<br>Blood Services<br>St. Paul Region<br>100 S. Robert St.<br>St. Paul, MN 55107<br>(612) 291-6789<br>(612) 291-6767 (night) |
| Michigan                | American Red Cross<br>Blood Services<br>Southeastern Michigan Region<br>100 Mack Ave.<br>P.O. Box 351<br>Detroit, MI 48232<br>(313) 494-2715     | Northern Illinois<br>(Chicago)                    | American Red Cross<br>Blood Services<br>Mid-America Region<br>43 E. Ohio St.<br>Chicago, IL 60611<br>(312) 440-2222                            |

APPENDIX 5. Varicella-zoster immune globulin—regional distribution centers —  
Continued

| Service area   | Regional center and 24-hour telephone   | Service area  | Regional center and 24-hour telephone   |
|--|---|---|---|
| Arkansas,<br>Kansas, Kentucky,<br>Missouri,<br>Southern Illinois | American Red Cross<br>Blood Services<br>Missouri-Illinois Region<br>4050 Lindell Blvd.<br>St. Louis, MO 63108<br>(314) 658-2000<br>(314) 658-2136 (night)   | Nevada, Utah,<br>Wyoming,<br>Northern<br>California | American Red Cross<br>Blood Services<br>Central California Region<br>333 McKendrie St.<br>San Jose, CA 95110<br>(408) 292-1626  |
| Nebraska   | American Red Cross<br>Blood Services<br>Midwest Region<br>3838 Dewey Ave.<br>Omaha, NE 68105<br>(402) 341-2723  | Alaska, Montana,<br>Oregon                          | American Red Cross<br>Blood Services<br>Pacific Northwest Region<br>4200 S.W. Corbett St.<br>Portland, OR 97201<br>(503) 243-5286   |
| Tennessee  | American Red Cross<br>Blood Services<br>Nashville Region<br>321 22nd Ave., N.<br>Nashville, TN 37203<br>(615) 327-1931, ext. 315  | Idaho   | American Red Cross<br>Blood Services<br>Snake River Region<br>5380 Franklin St.<br>Boise, ID 83705<br>(208) 342-4500  |
| Louisiana,<br>Oklahoma,<br>Texas                                 | Gulf Coast Regional<br>Blood Center<br>1400 La Concha<br>Houston, TX 77054-1802<br>(713) 791-6250<br><br>American Red Cross<br>Blood Services<br>Central Texas Region<br>McLennan County Chapter<br>4224 Cobbs Dr.<br>Waco, TX 76710<br>(817) 776-8754<br><br>American Red Cross<br>Blood Services<br>Red River Region<br>1809 Fifth St.<br>Wichita Falls, TX 76301<br>(817) 322-8686 | Washington  | Puget Sound Blood Center<br>Terry at Madison<br>Seattle, WA 98104<br>(206) 292-6525   |
| Colorado,<br>New Mexico  | United Blood Services<br>1515 University Blvd., N.E.<br>P. O. Box 25445<br>Albuquerque, NM 87125<br>(505) 247-9831  | Canada  | Canadian Red Cross<br>Blood Transfusion Service<br>National Office<br>95 Wellesley St. E.<br>Toronto, Ontario M4Y 1H6<br>(416) 923-6692   |
| Arizona  | American Red Cross<br>Blood Services<br>Southern Arizona Region<br>222 South Cherry Ave.<br>Tucson, AZ 85719<br>(602) 623-0541  | Puerto Rico   | American Red Cross<br>Servicio de Sangre Capitulo<br>GPO Box 6046<br>San Juan, PR 00936<br>(809) 759-7979   |
| Hawaii,<br>Southern<br>California                                | American Red Cross<br>Blood Services<br>L.A. -Orange Counties Region<br>1130 S. Vermont Ave.<br>Los Angeles, CA 90006<br>(213) 739-5200   | Central and<br>South America                        | South Florida Community<br>Blood Center<br>1675 N.W. Ninth Ave.<br>Miami, FL 33142<br>(305) 326-8888  |
|  |   | All other countries                                 | American Red Cross<br>Blood Services<br>Northeast Region<br>60 Kendrick St.<br>Needham, MA 02194<br>(617) 449-0773<br><br>American Red Cross<br>Blood Services<br>812 Huntington Ave.<br>Boston, MA 02115<br>(617) 731-2130 |



# **Immunization Recommendations for Health-Care Workers**

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
CENTERS FOR DISEASE CONTROL  
ATLANTA, GEORGIA 30333**

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## IMMUNIZATION RECOMMENDATIONS FOR HEALTH-CARE WORKERS

Because of their contact with patients or infective material from patients with infections, many health-care workers (including physicians, nurses, dental professionals, medical and nursing students, laboratory technicians, administrative staff, etc.) are at risk for exposure to and possible transmission of vaccine-preventable diseases. Maintenance of immunity is therefore an essential part of prevention and infection control programs for health-care workers. Optimal use of immunizing agents will not only safeguard the health of workers but also protect patients from becoming infected. A consistent program of immunizations could eliminate the problem of having susceptible health-care workers in hospitals and health departments and the attendant risks to other workers and patients.

- A. Administrative staff in any medical facility or health department providing direct patient care or contact are encouraged to formulate a comprehensive policy for all health-care workers. The following recommendations\* should be considered during policy development.

### 1. Influenza

To reduce staff illnesses and absenteeism during the influenza season and to reduce the spread of influenza from workers to patients, physicians, nurses, and other workers having extensive contact with patients having high-risk chronic medical conditions in health-care facilities or in the home setting should be immunized in the fall of each year. In addition, health-care workers with chronic medical conditions are at high risk for influenza-related complications, if infected and should be vaccinated against influenza.

Included in this category are:

- a. Those with chronic disorders of the cardiovascular or pulmonary systems requiring medical follow-up or hospitalization within the preceding year;
- b. Those with chronic metabolic disease (including diabetes), renal dysfunction, hemoglobinopathies, or immunosuppression.
- c. Any other health care worker 65 years of age and over.

\*Consult current Immunization Practices Advisory Committee (ACIP) recommendations for a detailed discussion of the rationale for each recommendation.

## 2. Hepatitis B

HBV infection is the major infectious occupational hazard for health care and public safety workers. The risk of acquiring HBV infection from occupational exposures is dependent on the frequency of percutaneous and permucosal exposures to blood or blood products. Any health care or public safety worker may be at high risk for HBV exposure depending on the tasks that he or she performs. If those tasks involve exposure to blood or blood contaminated body fluids on at least a monthly basis, then such workers should be vaccinated. Vaccination should be considered for other workers depending on the nature of the task.

Risks among health care professionals vary during the training and working career of each individual but are often highest during the professional training period. For this reason, it is recommended that vaccination be completed during training in schools of medicine, dentistry, nursing, laboratory technology, and other allied health professions.

- a. Persons at risk for hepatitis B virus infection who are demonstrated or judged likely to be susceptible should be actively immunized. Health-care workers who have contact with blood or blood products are at increased risk. These groups include (but are not limited to) physicians, nursing staff, dental professionals, and laboratory technicians.
- b. Before immunizing, serologic screening for hepatitis B need not be done unless the provider considers it cost-effective or the potential vaccinee requests it.
- c. Prophylaxis with an immune globulin (passive immunization) and vaccine (active immunization) should be used when indicated, such as following needle-stick or percutaneous exposure to blood that is at high risk for being HBsAg-positive. (See MMWR 1985;34:313-324, 329-335 for more details on post exposure prophylaxis.) Any needlestick exposure in an unvaccinated person should lead to initiation of the HB vaccine series.
- d. Immune globulins should not be used as a substitute when active immunization is indicated.

### 3. Measles

All persons susceptible by history or serology who are considered to be at increased risk for contact with patients infected with measles should be protected.\*

Most persons born before 1957 have probably been infected naturally and generally need not be considered susceptible. Younger persons can be considered immune only if they have documentation of:

- a. physician-diagnosed measles
- b. laboratory evidence of measles immunity
- c. adequate immunization with live measles vaccine on or after the first birthday.

Consideration should be given to administering measles vaccine in combination with rubella and mumps vaccines (measles-mumps-rubella [MMR] trivalent vaccine).

### 4. Mumps

All persons thought to be susceptible should be vaccinated unless otherwise contraindicated.\* Most persons born before 1957 are likely to have been infected naturally and generally need not be considered susceptible. Younger persons can be considered immune only if they have documentation of:

- a. physician-diagnosed mumps
- b. laboratory evidence of mumps immunity
- c. adequate immunization with live mumps vaccine when 12 or more months of age.

Consideration should be given to administering mumps vaccine in combination with measles and rubella vaccines (measles-mumps-rubella [MMR] trivalent vaccine).

### 5. Rubella

- a. All health-care workers (male or female) who are considered to be at increased risk for contact with patients with rubella or who are likely to have direct contact with pregnant patients should be immune to rubella.\*

\*Pregnancy is a contraindication to vaccination against measles, mumps, and/or rubella. Vaccine should not be given to pregnant women or those who may become pregnant within 3 months of vaccination.

- b. Before immunizing, serologic screening for rubella need not be done unless the health facility considers it cost-effective or the potential vaccinee requests it.
- c. Persons can be considered susceptible unless they have laboratory evidence of immunity or documented immunization with live virus vaccine on or after their first birthday.

Consideration should be given to giving rubella vaccine in combination with measles and mumps vaccines (measles-mumps-rubella [MMR] trivalent vaccine).

#### 6. Polomyelitis

- a. Routine primary immunization for adults in the United States is not recommended. Health-care workers who may have direct contact with patients who may be excreting polioviruses should complete a primary series. Primary immunization with enhanced potency inactivated polio vaccine (E-IPV) instead of oral polio vaccine (OPV) is recommended for these persons whenever feasible.

E-IPV is preferred because the risk for vaccine-associated paralysis following OPV is slightly higher in adults than in children and because workers may shed virus after OPV administration. Primary immunization with E-IPV consists of two doses at intervals of 1-2 months between doses, with a third dose 6-12 months after the second.

- b. In an outbreak, OPV should be provided to any health-care worker who has not been completely immunized or whose immunization status is unknown.\*

- B. Although health-care workers are not at substantially higher risk than the general adult population for acquiring diphtheria, pneumococcal disease, or tetanus, they should seek these immunizations from their primary care provider, according to the recommendations of the ACIP for adults.

#### 1. Tetanus and Diphtheria

After primary immunization, a tetanus-diphtheria booster is recommended for all persons every 10 years.

Primary immunization of adults consists of three doses of adult tetanus-diphtheria toxoid (Td): 4-6 weeks should separate the first and second doses, with the third dose given 6-12 months after the second.

\*Exceptions to this recommendation are discussed in the current ACIP recommendations under the heading Precautions and Contraindications: Immunodeficiency (reference 8).

## 2. Pneumococcal Disease

Personnel for whom pneumococcal vaccine is recommended include:

- a. Those with chronic illnesses, especially cardiovascular disease, chronic pulmonary disease, and diabetes mellitus.
  - b. Those with splenic dysfunction or anatomic asplenia, Hodgkins disease, lymphoma, multiple myeloma, cirrhosis, alcoholism, chronic renal failure, nephrotic syndrome, cerebral spinal fluid leaks, and other conditions, such as organ transplantation, associated with immunosuppression.
  - c. All otherwise healthy adults 65 years of age and older.
  - d. Persons living in special environments or social settings with an identified increased risk for pneumococcal disease or its complications (e.g. certain native - American populations.)
- C. Rabies vaccine may also be indicated for persons in high-risk groups, such as veterinarians, animal handlers, and certain laboratory workers. Smallpox vaccine should not be provided except to the very small number of people working with orthopox viruses.

Although hospitals and health departments need not assume responsibility for routine immunization of health-care workers against pertussis, tuberculosis, cholera, Japanese encephalitis, meningococcal disease, plague, rabies, typhoid, typhus, or yellow fever, vaccination against these diseases and administration of immune globulin to prevent hepatitis A should be considered when indicated for foreign travel.

## D. Other Issues

An immunization record should be maintained for all health-care workers reflecting both documented histories and immunizations administered at the provider site. At each immunization encounter, the record should be updated and the health-care workers encouraged to maintain the record as appropriate.

In addition to informing prospective health-care workers of any existing immunization policy, health facility administrative staff may wish to consider catch-up programs for health-care workers already employed. Since educational components will enhance the success of any immunization program, reference materials should be available to assist in answering questions regarding the diseases, vaccines, and toxoids, and the program or policy being implemented. To help ensure acceptance of the program goals, it may be necessary to conduct educational workshops or seminars several weeks prior to the initiation of the program.

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## F. ADVERSE EVENTS FOLLOWING IMMUNIZATION

Modern vaccines are very safe and effective, but not completely so. Adverse events following immunization have been reported with all vaccines. These range from frequent, minor local reactions to extremely rare, severe, systemic illness such as paralysis associated with OPV. Those involved in immunization programs have the responsibility to determine the real risk of these vaccines and to constantly weight these risks against the benefits of vaccine usage. Therefore, the post-marketing surveillance of vaccine for temporally associated events should be a high priority.

### Procedures for Handling Immediate Reactions

Anaphylaxis, a potentially life-threatening acute systemic allergic reaction to a foreign substance, is extremely uncommon after immunization. Nonetheless, immunization clinic staff should have basic knowledge on how to recognize and initiate immediate treatment of this reaction. Emergency procedures must be established by the medical director or medical consultant in each area and appropriate emergency drugs and equipment should be readily available at each clinic site. (See "sample orders": attachment of the Immunization Contract). If immunizations are given away from the regular clinic site (school clinics, mass clinics, patient's home, etc.) a policy should be in place that includes: 1) written medical orders, 2) emergency tray and procedures and 3) vaccine transport and storage.

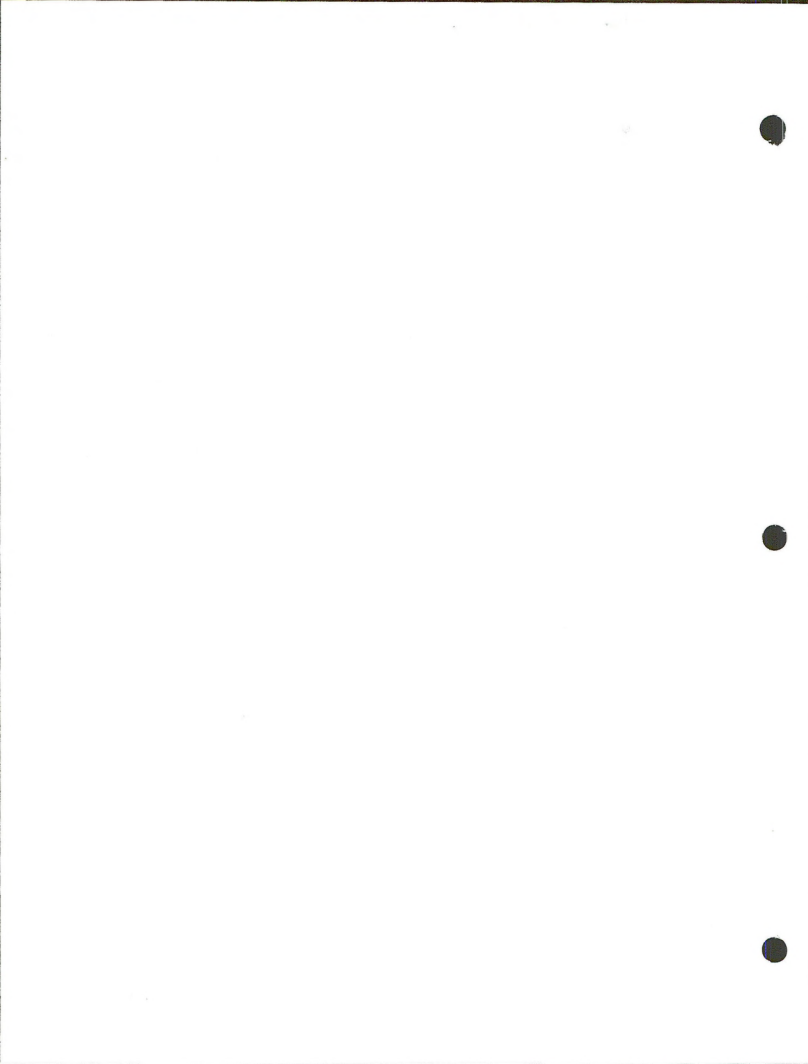
### Reporting Adverse Events

To improve knowledge about adverse reactions, all temporally associated events severe enough to require the recipient to seek medical attention should be evaluated and reported in detail to the Immunization Program in the appropriate format (see Immunization Contract). It is frequently impossible to establish cause-and-effect relationships when untoward events occur after receiving vaccine(s) since temporal association alone does not necessarily indicate causation.

Public vaccine providers are to report any illness that occurs within 30 days of vaccination and is serious enough to require hospitalization or a visit to a physician or public health facility. These reports are evaluated by the Adverse Reaction Coordinator and forwarded to CDC as appropriate for inclusion in national data. (For further discussion, see Section II - Vaccine Contract). A space for the telephone number to call if a reaction occurs is included on the Important Information Forms.

The form to record and report adverse events following immunization can be found attached to the vaccine contract.

Until 1989, reactions to vaccine that was purchased through private funds or administered at private clinics was not reported to the Immunization Program. Since March 21, 1988, all health care providers (public and private) are required by law to record permanently certain information and report selected events after vaccination as stated in the attached National Childhood Vaccine Injury Act. We now encourage all vaccine



providers to report vaccine reactions to the Immunization Program on the CDC Form 71.19 described below.

### The Reporting System

1. Important information statements contain a statement on the reporting of adverse reactions and to whom to report these. This initiates the reporting mechanism, if done.
2. The Vaccine Reaction Telephone Log (on the back side of the Monthly Vaccine Report Form) should be used to record all vaccine reaction-related phone calls -- serious or not. Those reports which are considered serious should be followed by a formal report on the form attached to the vaccine contract.
3. The Report of Adverse Event Following Immunization (CDC Form 71.19) is a multi-copy reporting form - only differences in the reporting form copies is that the patient identifying information is removed on the CDC copy. The provider should keep the appropriate copy and forward the others to the Montana Immunization Program.
  - a. There are instructions on the back of the form as to which cases should be reported: only if a reaction occurs within four weeks of receipt of a vaccine and was severe enough to require hospitalization or a visit to a physician or health facility.
  - b. Deaths or suspicious clusters are to be phoned to the Montana Immunization Program who will in turn call CDC.

### Decision to Continue Vaccinations

If a serious vaccine reaction has occurred, the decision to continue with further immunization should be made by an appropriate medical authority. Consultation with the medical consultant should occur if there is uncertainty whether to proceed with immunization or not.

### Clinical Features of Vaccine Reactions

Vaccine Reactions vary greatly in their symptoms and severity ranging from local reactions to neurologic reactions and death.

1. Local reactions - characterized by erythema and warmth at the injection site; are most common following DTP vaccine. Less common but of concern is the sterile abscess which may drain spontaneously or be drained surgically. When cultured it produces no growth.
2. Systemic reactions - such as fever occur together with a local reaction, present alone or together with another systemic, local or neurologic reaction. Other systemic reactions include rash, allergic reactions and arthritis/arthritis.
3. Neurologic reactions - are the most serious form of reaction as well as the rarest events associated with vaccines. When they occur they may



present as febrile or afebrile seizures, encephalitis, encephalopathy, paralysis, Guillain Bar're Syndrome, Peripheral neuritis or neuropathy or the rarer reactions; including optic neuritis with atrophy, transverse myelitis, cranial nerve palsey and unilateral deafness.

The occurrence of any reaction following the administration of a vaccine is in itself a complication. The neurologic events command the most attention due to their severity and potential for permanent sequalee.

#### Diagnosis

Most frequently we can make a temporal association, but not a casual relationship between vaccine and reaction. Except with local reactions occurring at the injection site, the occurrence of non-specific symptoms may or may not be due to the vaccine just administered.

We have learned, however, that certain kinds of symptoms are associated with specific vaccines. Fever is the most common of the reported symptoms. It occurs more immediately with the administration of killed vaccines and follows the incubation periods of the live virus vaccines but frequently with shorter periods.

For purposes of data collection - we encourage reports of vaccine associated adverse events where the recipient was ill enough to be taken to a health care provider and the onset of the symptoms occurred within 30 days of the administration of the vaccine. While these are arbitrary, they provide a reproducibility of the data - absolutely essential for meaningful analysis.

#### Epidemiology

Information on program and epidemiologic analysis of the reporting system is available from the Montana Immunization Program.

#### Closing Statement on Adverse Reactions Following Immunization

No vaccine is completely without adverse effects. In general, these reactions are mild and transient. In very rare instances, some serious events have been associated with a vaccine. Nevertheless, the overall benefits gained from preventing the disease are usually substantially greater than the potential risks of vaccination.



**National Childhood Vaccine Injury Act:  
Requirements for Permanent Vaccination Records and for  
Reporting of Selected Events After Vaccination**

Since March 21, 1988, health-care providers who administer certain vaccines and toxoids are required by law to record permanently certain information and to report certain events.\* The vaccines and toxoids to which these requirements apply follow: diphtheria and tetanus toxoids and pertussis vaccine (DTP); pertussis vaccine (P); measles, mumps, and rubella single-antigen vaccines and combination vaccines (MMR, MR); diphtheria and tetanus toxoids (DT); tetanus and diphtheria toxoids (Td); tetanus toxoid (T); poliovirus vaccine live, oral (OPV); and poliovirus vaccine inactivated (IPV) (Table 1). The requirements also will apply to DTP combined with inactivated poliovirus vaccine (DTP/Polio combined) if it becomes available.

**Requirements for Recording**

Specifically, all health-care providers who administer one or more of these vaccines or toxoids are required to ensure that there is recorded in the vaccine recipient's permanent medical record (or in a permanent office log or file) the date the vaccine was administered, the manufacturer and lot number of the vaccine, and the name, address, and title of the person administering the vaccine. The term health-care provider is defined as any licensed health-care professional, organization, or institution, whether private or public (including federal, state, and local departments and agencies), under whose authority a specified vaccine is administered.

**Requirements for Reporting**

Health-care providers are required to report to the U.S. Department of Health and Human Services (DHHS) selected events occurring after vaccination. Reportable events applicable to the previously mentioned vaccines and toxoids are shown in Table 1 and include events described in the vaccine manufacturer's package insert as contraindications to receiving additional doses of the vaccine.

**Methods for Reporting**

In the United States, vaccines are either publicly or privately purchased. Publicly purchased vaccines are bought with federal, state, and/or local government funds. At present, the method and route for reporting adverse events depend on whether the vaccine administered is publicly or privately purchased. Events occurring after receipt of publicly purchased vaccines are reported through local, county, and/or state health departments to the Centers for Disease Control (CDC) on its Report of Adverse Events Following Immunization (CDC form 71.19). Events occurring after receipt of a privately purchased vaccine usually are reported directly to the Food and Drug Administration (FDA) on its Adverse Reaction Report (FDA form 1639) by the health-care provider or the manufacturer.

For the time being, these two systems for reporting adverse events are to be used to implement the requirement of Title XXI of the Public Health Service Act for reporting adverse events to DHHS (Table 2).

Reportable events occurring after receipt of a publicly purchased vaccine shall be reported to local, county, and/or state health departments through channels currently in place at those institutions. The Report of Adverse Events Following Immunization, available at each state health department, shall be completed and sent by the state health department to CDC.

\*The National Childhood Vaccine Injury Act of 1986, at Section 2125 of the Public Health Service Act as codified at 42 U.S.C. § 300aa-25 (Supp. 1987).

**TABLE 1. Reportable events following vaccination**

| Vaccine/Toxoid | Event  | Interval from Vaccination  |
|----------------|--|--|
| DTP, P,        | A. Anaphylaxis or anaphylactic shock   | 24 hours   |
| DTP/Polio      | B. Encephalopathy (or encephalitis)*   | 7 days   |
| Combined       | C. Shock-collapse or hypotonic-hyporesponsive collapse*  | 7 days   |
|                | D. Residual seizure disorder*  | (See Aids to Interpretation*)  |
|                | E. Any acute complication or sequela (including death) of above events   | No limit   |
|                | F. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine† (such as convulsions) | (See package insert)   |
| Measles,       | A. Anaphylaxis or anaphylactic shock   | 24 hours   |
| Mumps, and     | B. Encephalopathy (or encephalitis)*   | 15 days for measles, mumps, and rubella vaccines; 7 days for DT, Td, and T toxoids |
| Rubella; DT,   |  | (See Aids to Interpretation*)  |
| Td, Tetanus    |  |  |
| Toxoid         | C. Residual seizure disorder*  | No limit   |
|                | D. Any acute complication or sequela (including death) of above events   | No limit   |
|                | E. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine†                       | (See package insert)   |
| Oral Polio     | A. Paralytic poliomyelitis   |  |
| Vaccine        | — in a non-immunodeficient recipient   | 30 days  |
|                | — in an immunodeficient recipient  | 6 months   |
|                | — in a vaccine-associated community case   | No limit   |
|                | B. Any acute complication or sequela (including death) of above events   | No limit   |
|                | C. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine†                       | (See package insert)   |
| Inactivated    | A. Anaphylaxis or anaphylactic shock   | 24 hours   |
| Polio          | B. Any acute complication or sequela (including death) of above event  | No limit   |
| Vaccine        | C. Events in vaccinees described in manufacturer's package insert as contraindications to additional doses of vaccine†                       | (See package insert)   |

**\*Aids to Interpretation:**

Shock-collapse or hypotonic-hyporesponsive collapse may be evidenced by signs or symptoms such as decrease in or loss of muscle tone, paralysis (partial or complete), hemiplegia, hemiparesis, loss of color or turning pale white or blue, unresponsiveness to environmental stimuli, depression of or loss of consciousness, prolonged sleeping with difficulty arousing, or cardiovascular or respiratory arrest.

Residual seizure disorder may be considered to have occurred if no other seizure or convulsion unaccompanied by fever or accompanied by a fever of less than 102 °F occurred before the first seizure or convulsion after the administration of the vaccine involved.

AND, if in the case of measles-, mumps-, or rubella-containing vaccines, the first seizure or convulsion occurred within 15 days after vaccination OR in the case of any other vaccine, the first seizure or convulsion occurred within 3 days after vaccination, AND, if two or more seizures or convulsions unaccompanied by fever or accompanied by a fever of less than 102 °F occurred within 1 year after vaccination.

The terms seizure and convulsion include grand mal, petit mal, absence, myoclonic, tonic-clonic, and focal motor seizures and signs. Encephalopathy means any significant acquired abnormality of, injury to, or impairment of function of the brain. Among the frequent manifestations of encephalopathy are focal and diffuse neurologic signs, increased intracranial pressure, or changes lasting at least 6 hours in level of consciousness, with or without convulsions. The neurologic signs and symptoms of encephalopathy may be temporary with complete recovery, or they may result in various degrees of permanent impairment. Signs and symptoms such as high-pitched and unusual screaming, persistent inconsolable crying, and bulging fontanel are compatible with an encephalopathy, but in and of themselves are not conclusive evidence of encephalopathy. Encephalopathy usually can be documented by slow wave activity on an electroencephalogram.

†The health-care provider must refer to the CONTRAINDICATION section of the manufacturer's package insert for each vaccine.



Reportable events occurring after receipt of a privately purchased vaccine shall be reported by the health-care provider directly to the FDA on the Adverse Reaction Report (FDA form 1639). Health-care providers will need to ensure that the name of the vaccine manufacturer, the lot number of the vaccine, and the interval between vaccination and onset of the reaction are included on this form. FDA form 1639 can be obtained directly from Food and Drug Administration, HFN-730, Rockville, Maryland 20857. The form also is printed in *FDA Drug Bulletin*, the physician's edition of the *Physicians' Desk Reference*, *USP Drug Information for Health Care Providers*, and *AMA Drug Evaluations* and can be duplicated.

Health-care providers are requested not to provide the names and other personal identifiers of patients on FDA form 1639. Such information will be reported for publicly purchased vaccines to state and local health departments, which in turn will remove the names and personal identifiers when submitting CDC form 71.19 to CDC.

Reported by: National Vaccine Program, Office of the Assistant Secretary of Health, Office of Biologics, Office of Epidemiology and Statistics, Food and Drug Administration, Div of Immunization, Center for Prevention Services, CDC.

**TABLE 2. Reporting of events occurring after vaccination**

|                                      | Vaccine Purchased<br>with Public Money  | Vaccine Purchased<br>with Private Money  |
|--------------------------------------|---|--|
| <b>Who Reports:</b>                  | Health-care provider who administered the vaccine   | Health-care provider who administered the vaccine  |
| <b>What Products<br/>To Report:</b>  | DTP, P, Measles, Mumps, Rubella, DT, Td, T, OPV, IPV, and DTP/Polio Combined  | DTP, P, Measles, Mumps, Rubella, DT, Td, T, OPV, IPV, and DTP/Polio Combined   |
| <b>What Reactions<br/>To Report:</b> | Events listed in Table 1 including contraindicating reactions specified in manufacturers' package inserts               | Events listed in Table 1 including contraindicating reactions specified in manufacturers' package inserts                                      |
| <b>How To<br/>Report:</b>            | Initial report taken by local, county, or state health department. State health department completes CDC form 71.19     | Health-care provider completes Adverse Reaction Report-FDA form 1639 (include interval from vaccination, manufacturer, and lot number on form) |
| <b>Where To<br/>Report:</b>          | State health departments send CDC form 71.19 to:<br>MSAEFI/IM (E05)<br>Centers for Disease Control<br>Atlanta, GA 30333 | Completed FDA form 1639 is sent to:<br>Food and Drug<br>Administration (HFN-730)<br>Rockville, MD 20857  |
| <b>Where To<br/>Obtain Forms:</b>    | State health departments  | FDA and publications such as <i>FDA Drug Bulletin</i>  |

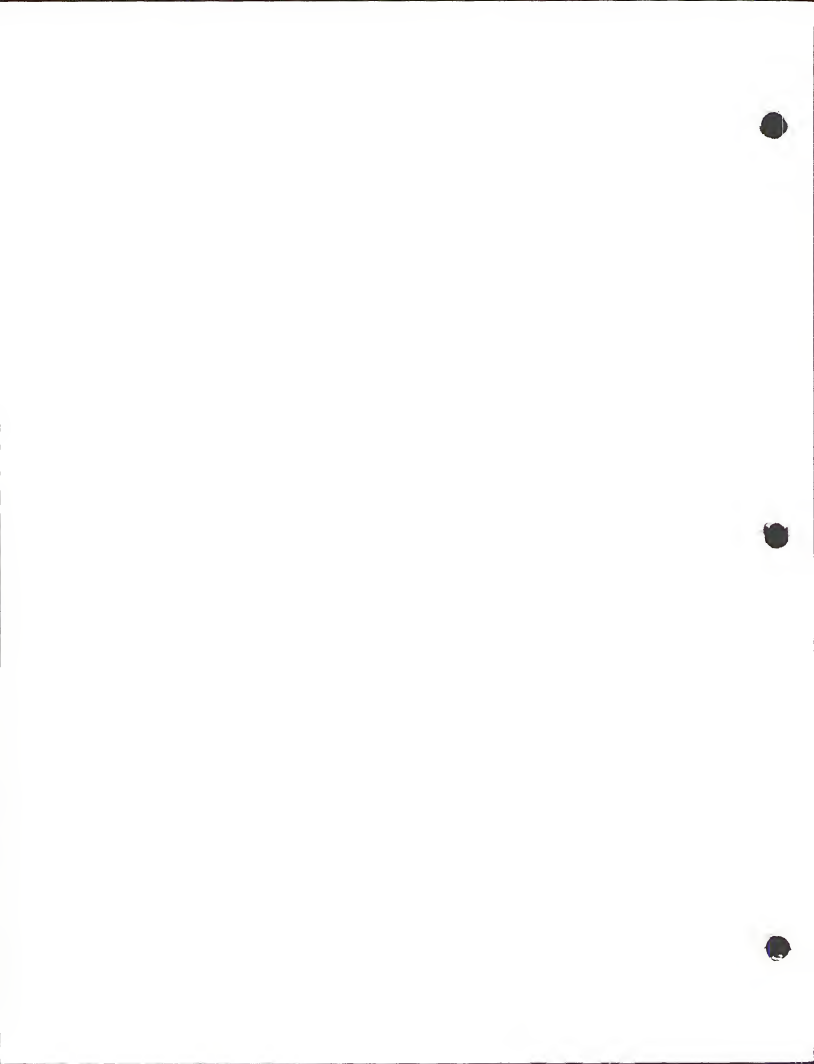


TAB VIII

TOPIC

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|                                   |   |
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| References and Addresses. . . . . | 1 |
|-----------------------------------|---|



## References and Reference Addresses

The following is a list of references used in developing the Montana Immunization Manual:

1. Recommendations of the Immunization Practices Advisory Committee (ACIP).  
Published by:  
    U.S. Department of Health and Human Services  
    Public Health Service  
    Centers for Disease Control  
    Atlanta, GA 30333
2. The Report of the Committee on Infectious Diseases, "The Red Book,"  
    authored by the Committee on Infectious Diseases, American Academy of  
    Pediatrics, 20th Edition, 1986. See Tab V.
3. Health Information for International Travel, 1987. Published by U.S.  
    Department of Health and Human Services, Public Health Service, Centers  
    for Disease Control. See Tab V.
4. Control of Communicable Diseases in Man, 14th Edition, 1985. Abram S.  
    Benenson, Editor. An official report of The American Public Health Asso-  
    ciation.  
    The American Public Health Association  
    1015 15th Street, N.W.  
    Washington, D.C. 20005
5. Morbidity and Mortality Weekly Report (MMWR), published by the U.S.  
    Department of Health and Human Services, Public Health Service, Centers  
    for Disease Control, Atlanta, GA.
6. The American College of Obstetricians and Gynecologists (ACOG). See Tab  
    V.
7. The Guide for Adult Immunization (1985), authored by the American College  
    of Physicians. See Tab V.
8. Colorado Department of Health Immunization Manual.
9. Louisiana Immunization Policies and Procedures Manual.
10. South Dakota Immunization Manual.

REP/vg-2c



V A C C I N E   C O N T R A C T

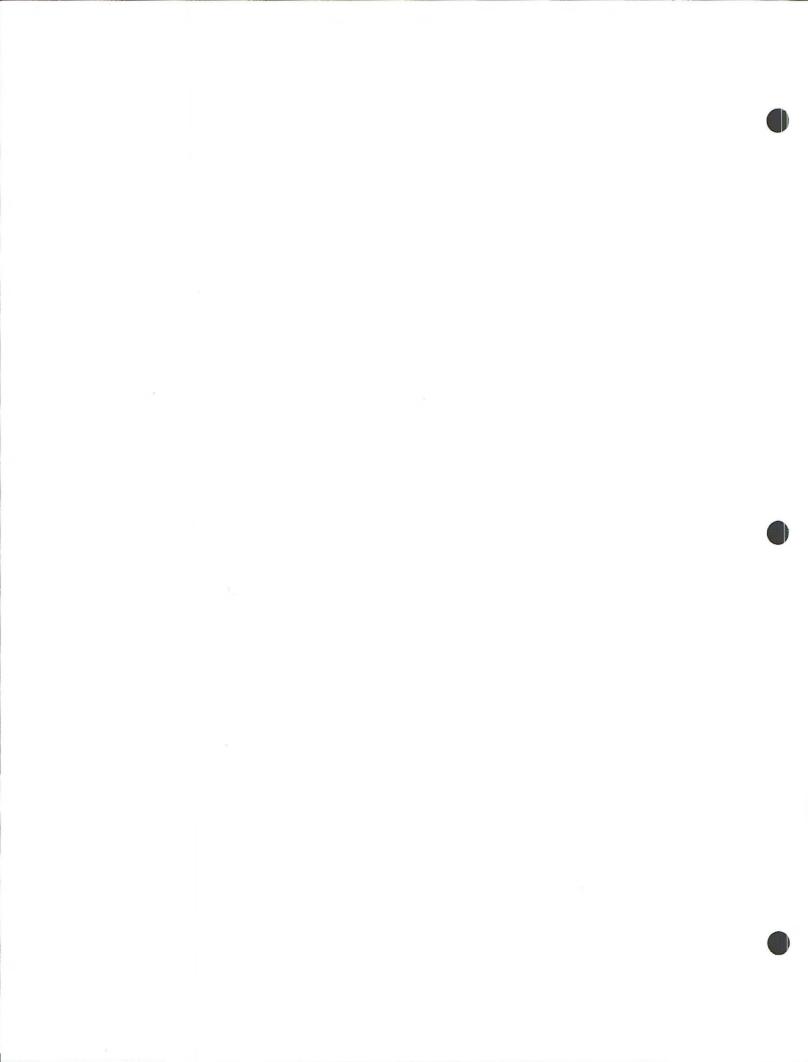
Prepared by:

MONTANA IMMUNIZATION PROGRAM

Department of Health and Environmental Sciences  
Health Services Division  
Helena, Montana 59620  
(406) 444-4740

Revised 7-26-89

VACC-TRK





## VACCINE CONTRACT

The following Contract is made between the Montana Department of Health and Environmental Sciences (DHES) and \_\_\_\_\_ (Contractor).

### I. PURPOSE OF CONTRACT

The purpose of this Contract is to provide the Contractor with vaccines and program supplies for local immunization activities, while establishing the guidelines and conditions for their use.

### II. DURATION OF CONTRACT

This Contract will take effect the date it is signed by both parties and will continue until either party receives written notice that it is terminated, effective 30 days after the date it is either mailed or personally delivered to the other party.

### III. RESPONSIBILITIES OF THE DEPARTMENT OF HEALTH AND ENVIRONMENTAL SCIENCES

DHES shall, to the extent that federal and state immunization funds allow:

(1) Provide Contractor with vaccines and up-to-date immunization informational materials, including current recommendations from the Public Health Service's Advisory Committee on Immunization Practices (ACIP), and forms for comprehensive local childhood immunization activities.

(2) Provide technical assistance on immunization activities.

(3) Provide in-service or formal training programs on vaccine-preventable diseases, vaccine administration, or other related program activities, as necessary or upon request.

(4) Promote and distribute the Official Montana Immunization Record.

(5) Provide materials and technical assistance to implement patient tracking and recall systems locally.

(6) Provide the Contractor with a placard indicating vaccine will not be denied because of inability to pay any administrative fee charged.

(7) Maintain a state measles and suspect measles registry; monitor or participate in measles case investigations; provide outbreak control assistance; and implement active surveillance programs as appropriate.

(8) Provide epidemiologic feedback on measles disease investigations.



(9) Maintain the state register for the "Adverse Reaction Monitoring System" and forward reports of serious adverse reactions to the Centers for Disease Control.

(10) Monitor and recall vaccines suspected of causing adverse reactions.

(11) Maintain a vaccine distribution and usage log for each provider.

(12) Tabulate monthly vaccine usage reports for statewide usage data.

(13) Provide the Contractor, upon request, with sample standing medical orders, and review medical orders developed by the Contractor for administration of vaccine.

(14) Perform on-site clinic review as soon as possible after this Contract is signed by both parties, and once per calendar year thereafter, following procedures outlined in this Contract.

#### IV. RESPONSIBILITIES OF CONTRACTOR

As a condition of receiving and using vaccine provided by DHES, the Contractor agrees to do the following (DHES may cease to supply Contractor with vaccine if Contractor does not comply with the responsibilities stated below):

##### A. Vaccine Administration

(1) Assure current written medical orders exist and are utilized during all immunization clinics for administration of vaccines and for emergency procedures in event of adverse reaction to a vaccine. Written medical orders must:

(a) Be reviewed annually;

(b) Follow recommendations compatible with those currently approved by the ACIP and/or the American Academy of Pediatrics (AAP) for indications of use, dosage, and route of all vaccines and combinations of vaccines;

(c) Specify those persons authorized to perform emergency procedures in event of adverse reaction and to administer vaccines;

(d) Be provided to DHES immediately after signing this Contract and annually thereafter;

(e) Be reviewed and/or rewritten and dated whenever changes in personnel occur.

(2) Refrain from charging patients for the cost of DHES-provided vaccines or from denying such vaccine to anyone for failure to pay an administrative fee. Any administrative fee must not exceed whatever amount is reasonable for such a service, and must be posted, along with the placard referred to in Section III(6), in a conspicuous location for client viewing.



(3) Submit to DHES by the 5th day of each month a Vaccine Report Form HES-III (Exhibit I) covering the prior month.

B. Vaccine Information

(1) Ensure that current ACIP recommendations are available to and utilized by clinic staff.

(2) Ensure that each person (or parent/guardian of that person) to whom vaccine is administered is adequately informed about the purpose and effect of each vaccine by doing the following:

(a) Provide a copy of the appropriate current "Important Information" sheet contained in Exhibit A of this Contract to each person to whom vaccine is administered, and/or that person's parents or guardians.

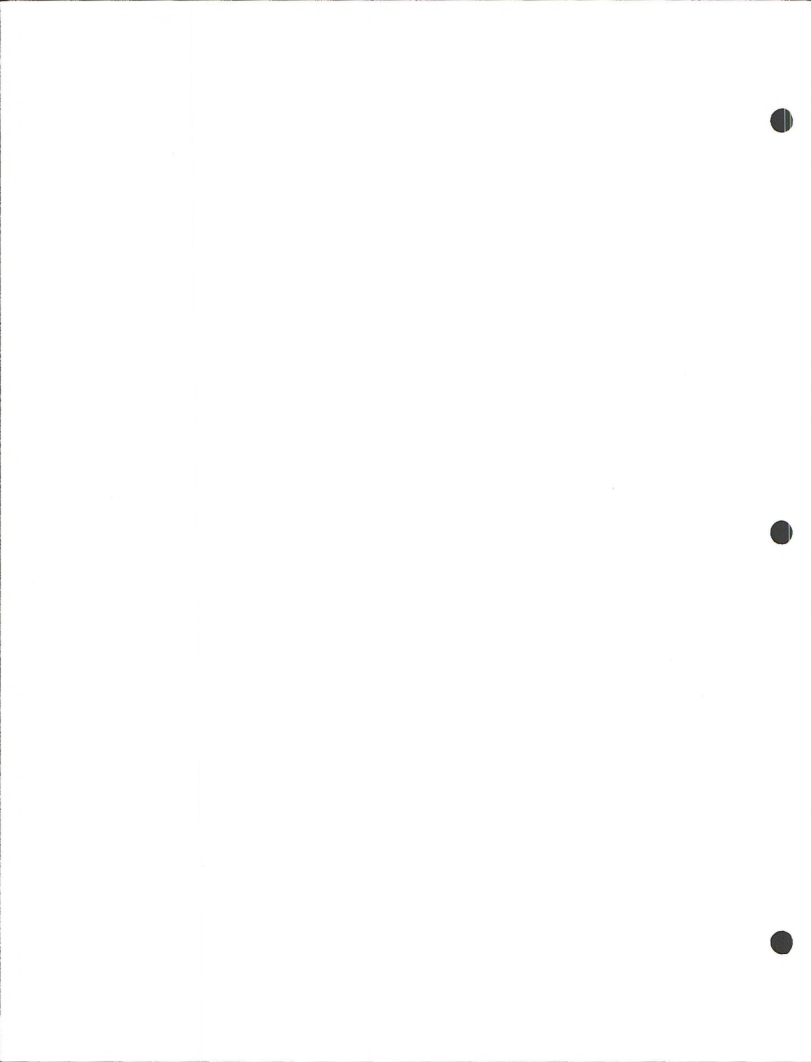
(b) Provide translated copies of the "Important Information" sheets when the vaccinees and/or their parents/guardians are not proficient in English. (Translations of the sheets are available in Spanish, French, Vietnamese, and Chinese from DHES upon request.)

(c) Give vaccinees and/or their parents/guardians the time and opportunity to read the "Important Information" sheets and to ask questions prior to administration of vaccine(s).

(d) Obtain the signature of each vaccinee and/or a parent/guardian in order to document the receipt of an "Important Information" sheet relating to each disease for which vaccine is furnished or administered. The lower portion of the "Important Information" sheet or a log sheet or signature card (Exhibit B) may be used.

(i) The following minimum information must be contained in the document signed by the vaccinee or the vaccinee's parent/guardian:

"I have read the information contained in the 'Important Information' form(s) about the disease(s) and the vaccine(s). I have had a chance to ask questions which were answered to my satisfaction. I believe I understand the benefits and the risks of the vaccine(s) and request that the vaccine(s) indicated below be given to me or to the person named for whom I am authorized to make this request."



(ii) In addition, the following entries must be completed: Name of vaccinee; his/her address; date of birth, and age; type of vaccine(s) administered; clinic identification; date of vaccination; site of vaccination; manufacturer and lot number for each vaccine; signature of person to receive the vaccine or person authorized to make the request; date of signature; and effective date of the appropriate "Important Information" form (printed on the form).

(e) Give the upper portion of the "Important Information" form appropriate for each vaccine received to the vaccinees and/or parents/guardians before they leave the clinic.

(f) Retain the signed portion of the "Important Information" forms, signed log sheets, and/or signature cards until notice is received in writing from DHES that retention is no longer required, and provide DHES, upon request, with a copy of any such documentation.

(g) Establish and ensure the use of a protocol for answering questions in any case where the information form is to be read and signed, in advance of the vaccination, by a parent, guardian, or other authorized person who will not be present at the site when the vaccination is given.

C. Personal Immunization Record

(1) Provide each vaccinee and/or parent/guardian with a signed and dated personal immunization record or update an existing record for each vaccine administered. The OFFICIAL MONTANA IMMUNIZATION RECORD is recommended. (Exhibit C).

(2) Advise each vaccinee or parent/guardian in writing (preferably on the Official Montana Immunization Record) of the date the next immunization(s) should be given.

D. Patient Tracking and Recall System

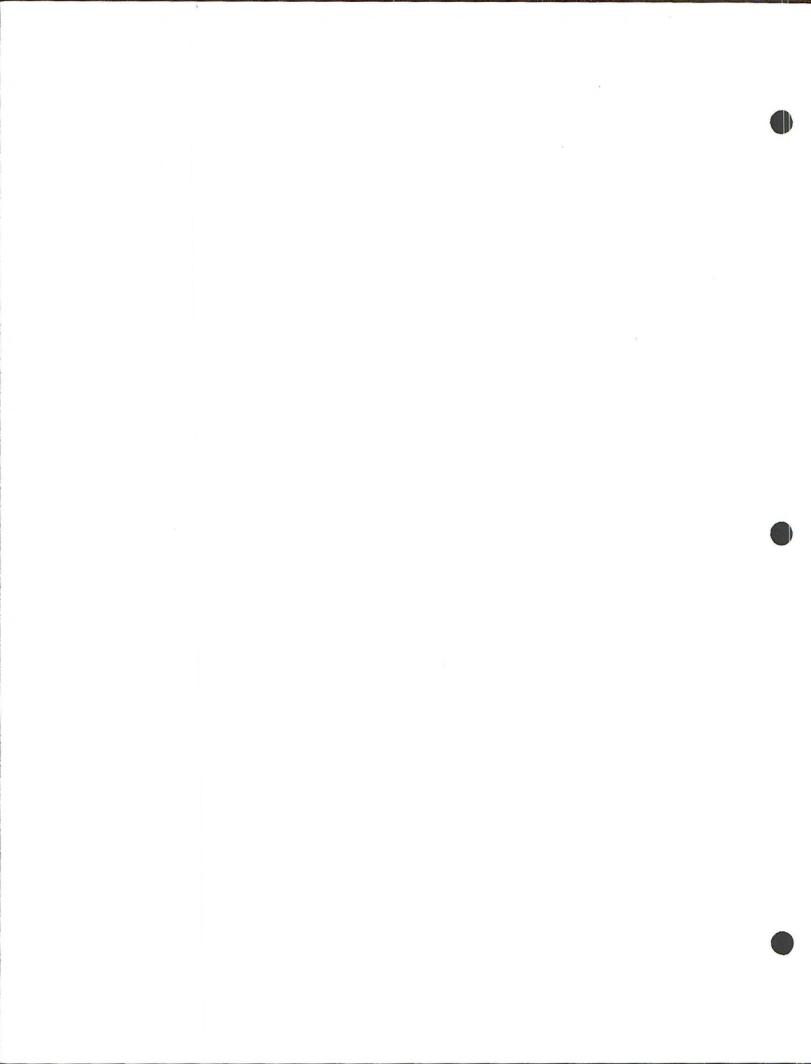
Establish and maintain a patient tracking and recall system to assure the vaccinees are immunized appropriately for their ages.

E. Vaccine Reactions

(1) Provide vaccinees and/or parents/guardians with a telephone number for reporting reactions following vaccination, either in the designated space on the appropriate vaccine "Important Information" sheets or on a form developed by the Contractor.

(2) Maintain a monthly vaccine reaction log (HES-

*This clause is not in facilities which do not require a recall system. - (Fam. Plan., Student Hlth. Serv., Job corps)*





111, Exhibit D) and, by the 5th of each month, forward to DHES a copy of this log with the vaccine report form for the prior month.

(3) Report to DHES' Immunization Program by telephone (444-4740) each case in which a vaccinee became ill within 4 weeks after administration of the vaccine and the illness was severe enough to cause death or to require hospitalization or a visit to a physician or other health care personnel. In addition, in each such case, submit to DHES by mail, immediately after the phone call, a completed CDC form, "Report of Adverse Event Following Immunization" (Exhibit E), for the incident.

#### F. Vaccine Handling and Storage

(1) Store vaccines in accordance with manufacturers' recommendations and the current RECOMMENDATIONS FOR HANDLING AND STORAGE OF SELECTED BIOLOGICALS (Exhibit L).

(2) Follow the refrigeration recommendations contained in Exhibit K.

(3) Maintain and keep on file a temperature monitoring log (HES-115) each working day which indicates daily temperatures (Exhibit F).

(4) If vaccine is to be administered at a site away from the usual storage site, transport it in a manner which will ensure the temperature is maintained in accordance with manufacturers' recommendations.

(5) Take measures to ensure that vaccine wastage/loss during each state fiscal year is kept to less than 5%, such measures to include:

(a) Monitoring vaccine expiration dates;

(b) Ensuring that vaccine shipments ordered from DHES' Immunization Program which are not delivered directly to the Contractor are picked up at the time and place designated by DHES and taken to the clinic site for storage in refrigeration or freezer units; and

(c) Notifying DHES' Immunization Program of the impending expiration of any vaccine at least 60 days before that date.

(6) Order all vaccines (see Exhibit G) in amounts adequate for at least a 3-month supply, and notify DHES' Immunization Program immediately whenever a vaccine shipment is received by signing and returning a copy of the HES-110 Vaccine Shipment Receipt Form (Exhibit H). [Note: Vaccine will not be shipped during the months of July and August because adequate shipping conditions cannot be guaranteed during the summer months.]

(7) Return to DHES all reusable vaccine shipping containers within 7 days of receipt of vaccine.

(8) Return any expired vaccine to the DHES Immunization Program.



G. Excessive Vaccine Loss; Replacement

If 5% or more of the total vaccine sent to the Contractor during any state fiscal year is lost or otherwise rendered unusable, unless the loss is due to actions by an entity other than the Contractor, Contractor will, at DHES' request, replace the lost vaccine and submit to DHES a copy of the invoice(s) for the replacement vaccine.

V. CLINIC REVIEW

This Contract will be reviewed at least once each calendar year according to the following steps, in order to determine whether it should be continued or terminated:

(1) A representative of DHES' Immunization Program will arrange a time with the Contractor to conduct a clinic review (Exhibit J). The Contractor or the Contractor's designee will be present during the review.

(2) DHES' representative will review each policy and procedure addressed in the section on "Responsibilities of the Contractor".

(3) If no deficiencies are identified, and the Contractor has had the opportunity to comment on, and is satisfied with, the review, both the Contractor and the reviewer may sign and date the completed review form.

(4) If deficiencies are identified, the representative will discuss with the Contractor action necessary to correct the deficiencies. The representative will make follow-up contact within 30 days following the clinic review to determine if the deficiencies have been corrected. If they have not, DHES may deny the Contractor vaccine until DHES is satisfied the deficiencies have been corrected or may terminate the Contract entirely.

(5) DHES will give the Contractor a copy of the completed clinic review form, and the original will be kept by DHES, along with a copy of the Contractor's current medical orders.

VI. TERMINATION

The Contractor may terminate this Contract for any reason, at any time, by sending written notice to that effect to DHES. DHES may terminate this Contract if:

(1) Federal or state funding is inadequate to supply Contractor with vaccine;

(2) The Contractor violates any of its duties stated in this Contract; or

(3) The Contractor is no longer providing vaccination services.



## VII. MODIFICATIONS AND PREVIOUS AGREEMENTS

This instrument contains the entire Contract between the parties, and no statements, promises, or inducements made by either party or agent of either party which are not contained in this written Contract are valid or binding. This Contract may not be enlarged, modified, or altered except in writing, signed by the parties. No change, addition, or erasure of any printed portion of this Contract is valid or binding upon either party.

## VIII. AUDITING AND ACCESS TO RECORDS

The Contractor agrees to maintain records of the activities covered by this Contract and to allow access to them by DHES and, in addition, the legislative auditor as may be necessary for legislative audit and analysis purposes in determining compliance with the terms of this Contract, in determining compliance with the terms of this Contract, as required by Section 5-13-304, Montana Code Annotated. Notwithstanding the provisions of Section VI, this Contract may be terminated upon any refusal of the Contractor to allow the access to records referred to above.

## IX. HOLD HARMLESS AND INDEMNIFICATION

The Contractor shall hold harmless and indemnify DHES for any liability, claims, demands, costs, and actions at law arising out of its performance of this Agreement to the extent that the liability, claim, demand, cost, action, or damages are caused by or arise out of the acts or negligence of the Contractor or its employees or agents.

## X. SEVERABILITY

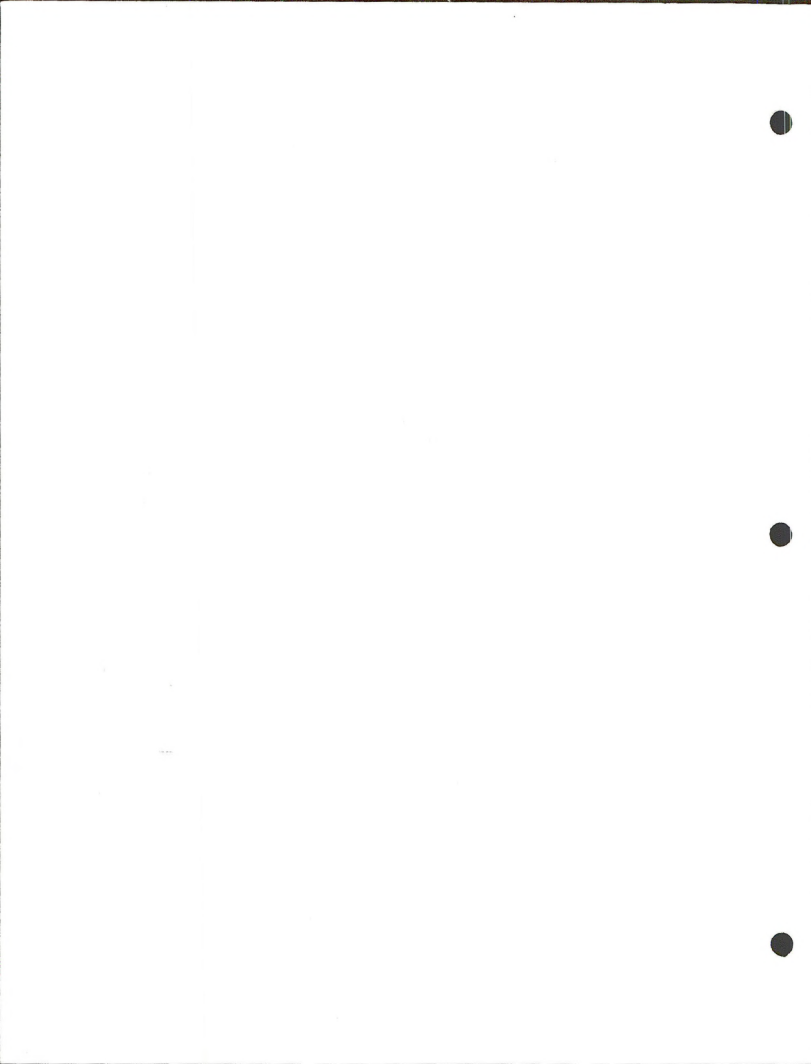
It is understood and agreed by the parties hereto that if any term or provision of this Contract is by the courts held to be illegal or in conflict with any Montana law, the validity of the remaining terms and provisions is not affected, and the rights and obligations of the parties will be construed and enforced as if the Contract did not contain the particular term or provision held to be invalid.

## XI. LIAISONS

The Contractor's liaison to DHES for purposes of this Contract is the following person or that person's successor at the Contractor's address noted below:

\_\_\_\_\_  
Name

\_\_\_\_\_  
Title



DHES' liaison to the Contractor for purposes of this Contract is Richard Paulsen or his successor at DHES, Cogswell Building, Capitol Station, Helena, Montana 59620 [phone: 444-4740].

XII. EXECUTION

This Agreement consists of 9 pages and 12 Exhibits. The original is to be retained by DHES' Immunization Program. A copy of the original has the same force and effect for all purposes as the original.

To express the parties' intent to be bound by the terms of this Contract, they have executed this document on the dates set out below:

\_\_\_\_\_ BY: \_\_\_\_\_  
Date  
\_\_\_\_\_  
Print Name and Title  
\_\_\_\_\_  
\_\_\_\_\_  
Address  
\_\_\_\_\_  
Telephone Number

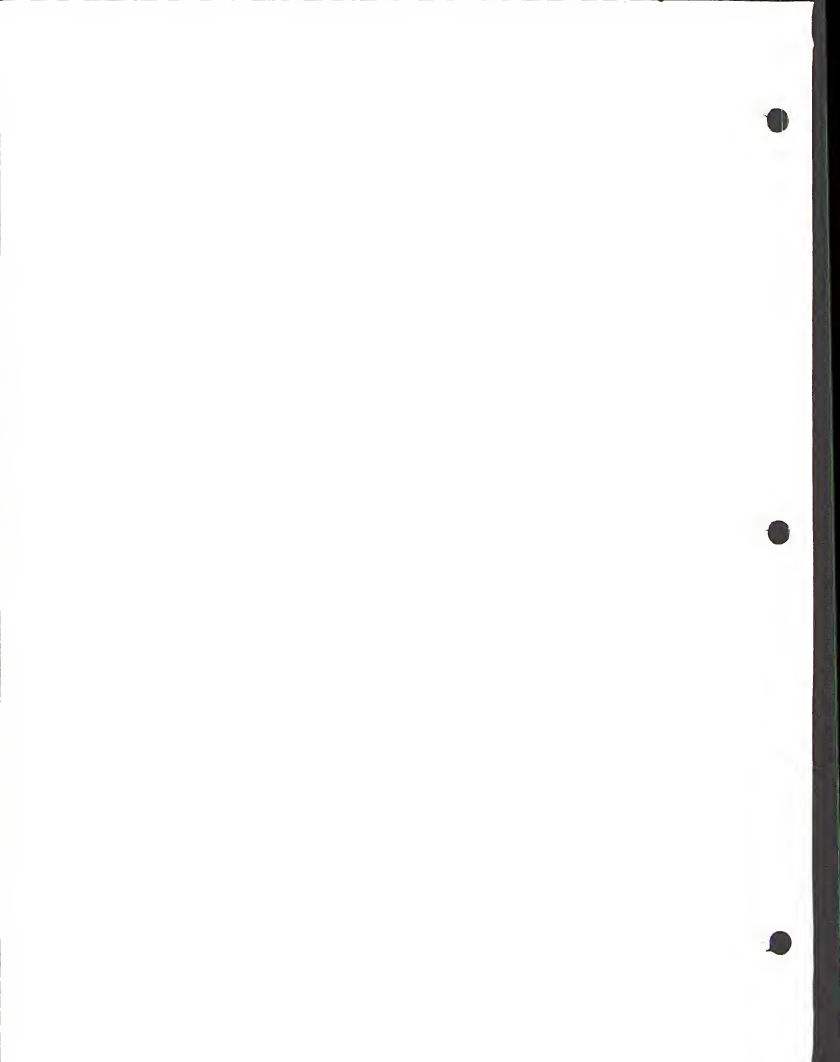
DEPARTMENT OF HEALTH AND ENVIRONMENTAL SCIENCES

\_\_\_\_\_ BY: \_\_\_\_\_  
Date RAYMOND J. HOFFMAN  
Administrator, Centralized  
Services Division

Approved for legal content by:

Eleanor A. Parker  
Eleanor A. Parker  
DHES Counsel

July 26, 1989  
Date





EXHIBITS

- A. Important Information Forms:
  - (1) Polio
  - (2) DPT/DT/Td
  - (3) Measles, Mumps, Rubella
  - (4) Haemophilus b Conjugate
- B. Instructions - Immunization Record and Signature Card
- C. Official Montana Immunization Record
- D. Vaccine Reaction Telephone Log (HES-111; flip side of I below)
- E. Report of Adverse Event Following Immunization (CDC/71.19)
- F. Temperature Monitoring Log (HES-115)
- G. Vaccine Order Blank (HES-108)
- H. Vaccine Shipment Receipt Form (HES-110)
- I. Vaccine Report Form (HES-111; flip side of D above)
- J. Clinic Review Form (HES-116)
- K. Refrigeration Recommendations
- L. Recommendations for Handling and Storage of Selected Biologicals

